Southern Medical Journal

JOURNAL OF THE SOUTHERN MEDICAL ASSOCIATION

VOL. 53 JULY 1960 NO. 7

In this issue–

THE CLINICAL USEFULNESS OF THE DYE DILUTION CURVE—Robert H. Franch 821

PHYSIOLOGIC BOWING OF THE LEGS—Mary Sherman 830

THE CONTROL OF INTRACTABLE PELVIC HEMORRHAGE BY LIGATION OF THE HYPOGASTRIC ARTERY—Samuel S. Binder and George A. Mitchell 837

EVALUATION OF DIAGNOSTIC PROCEDURES IN THE CLINICAL DIAGNOSIS OF GASTRIC CANCER—M. Frank Sohmer, David Cayer, and Zelma A. Kalnins 844

DRUG REACTIONS: REPORT OF 150 CASES—Mason I. Lowance 850

TONOGRAPHY IN OFFICE PRACTICE—Joseph H. Derivaux 853

CASE REPORT

CLOSTRIDIAL GAS GANGRENE AND SEPTICEMIA COMPLICATING LEUKEMIA—Lewis E. Jones, Wolfgang A. Wirth, and Cyrus C. Farrow 863

CASE REPORT

ROCKY MOUNTAIN SPOTTED FEVER WITH THROMBOCYTOPENIA—Carey W. Phillips, Jr., George T. Kimbrough, Jerome A. Weaver, and Alex L. Tucker 867

SEXUAL BEHAVIOR OF MANIC PATIENTS: A PRELIMINARY REPORT—J. B. Allison and W. P. Wilson 870

COMPLICATIONS OF PRESSOR AMINE THERAPY—Edward R. Dorney 875

CHOICE OF AGENTS FOR PREOPERATIVE PREPARATION OF THE COLON—Isidore Cohn, Jr. 881

Continued on cover 2

Fifty-Fourth Annual Meeting, October 31-November 3, 1960, St. Louis, Missouri

JULY 1960

VOLUME 53 NUMBER 7

Southern Medical Journal

JOURNAL OF THE SOUTHERN MEDICAL ASSOCIATION

STAFF

Editor
R. H. Kampmeier, M.D.

Managing Editor and Business Manager
Robert F. Butts

EDITORIAL BOARD

Surgery
William F. Rienhoff, Jr., M.D.

Neurology Psychiatry
Sullivan G. Bedell, M.D.

Orthopedics
Lenox D. Baker, M.D.

Proctology
Curtice Rosser, M.D.

Obstetrics Gynecology
Willis E. Brown, M.D.

Pediatrics
Preston A. McLendon, M.D.

Urology
Charles Rieser, M.D.

Dermatology
John H. Lamb, M.D.

Pathology
J. F. A. McManus, M.D.

General Practice
Stanley A. Hill, M.D.

OFFICERS

President
Edwin H. Lawson, M.D.

President-Elect
Tom D. Spies, M.D.
(Deceased Feb. 28, 1960)

First Vice-President
A. Clayton McCarty, M.D.

Second Vice-President
Jack C. Norris, M.D.

Published monthly by the Southern Medical Association, 2601 Highland Avenue, Birmingham 5, Alabama. Annual subscription, $10.00. Single copies, $1.00 each. **Copyright, Southern Medical Association, 1960.**

Entered as second-class matter at the Post Office at Birmingham, Alabama, under Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized December 20, 1921.

CONTENTS

Continued from cover 1

EXAGGERATION OF SYMPTOMS, MALINGERING, AND CONVERSION REACTION—Arthur M. Pruce, Maurice L. B. Clarke, and Henry J. Climo 885

CASE REPORTS

THE LATE STAGE OF THE MYELOPROLIFERATIVE SYNDROME: CASE REPORTS—John V. Denko 896

THE NEW OBSTETRIC PATIENT—George S. Allen 901

THE ELDERLY PATIENT: A CHALLENGE IN SURGICAL MANAGEMENT —William Riley Bosien and Marian Kreider Bosien 904

THE STAPHYLOCOCCUS PROBLEM ON A SINGLE DERMATOLOGIC WARD: CHARITY HOSPITAL—JANUARY-JUNE 1959—C. Barrett Kennedy, A. E. Caroe, and V. Medd Henington 910

CASE REPORT

BRAIN TUMORS IN THE NEWBORN—R. L. DeSaussure, Joe H. Miller, and C. E. Strickland 918

CASE REPORT

STAPHYLOCOCCAL ORBITAL SEPSIS IN NEWBORN INFANTS—Ray Hepner and David Hagar 922

DUAL BONE GRAFT FOR CONGENITAL PSEUDARTHROSIS OF THE TIBIA: VARIATIONS OF TECHNIC—George D. Purvis and J. E. Holder 926

EDITORIAL 932

The General Hospital and the Care of the Mentally Ill

TWENTY-FIVE YEARS AGO 933

SOUTHERN MEDICAL NEWS 934

KNOW YOUR SOUTHERN MEDICAL ASSOCIATION 936

BOOK REVIEWS 939

INSTRUCTIONS TO CONTRIBUTORS 939

INDEX TO ADVERTISERS Adv. Page 80

Southern Medical Journal

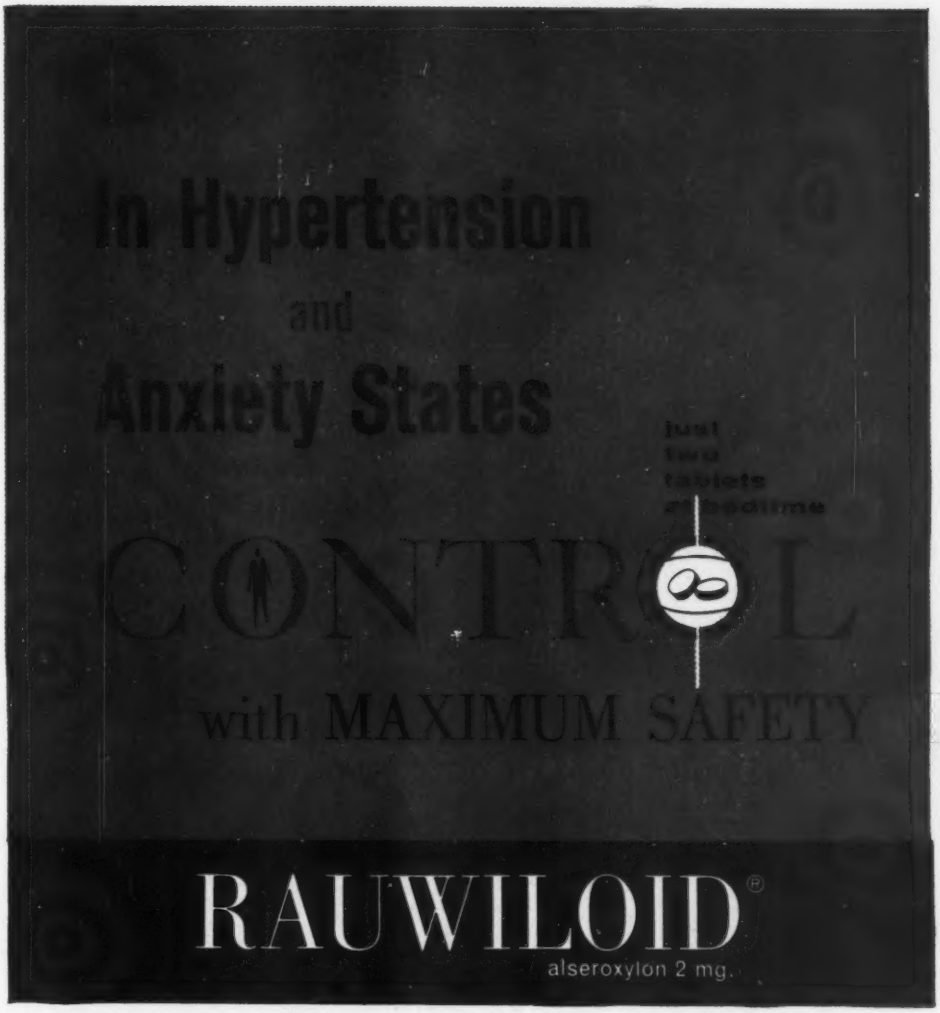
JOURNAL OF THE SOUTHERN MEDICAL ASSOCIATION

885
896
901
904
910
918
922
926
932
933
934
936
939
939
80

EDITOR, R. H. KAMPMEIER, M.D.
VANDERBILT UNIVERSITY SCHOOL OF MEDICINE
NASHVILLE, TENNESSEE

VOLUME 53 NOS. 1-12, 1960

SOUTHERN MEDICAL ASSOCIATION
2601 HIGHLAND AVENUE
BIRMINGHAM, ALABAMA



In Hypertension
Simplicity of control based on negligible incidence of serious side actions, simplicity of dosage, and applicability to a wide range of patients.

In Anxiety States
Rauwiloid is outstanding for its calming, nonsoporific sedation in anxiety states...with or without hypertension.

Compatible with other antihypertensive medications. Potentiates therapeutic action of more potent agents and permits their use in reduced and better tolerated dosage.

When more potent hypotensive action is needed, prescribe one of these convenient single-tablet combinations

***Rauwiloid*® + *Veriloid*®**
alseroxylon 1 mg. and alkavervir 3 mg.

or

Rauwiloid*® + *Hexamethonium
alseroxylon 1 mg. and hexamethonium chloride dihydrate 250 mg.

Patients with severe hypertension often can be maintained on Rauwiloid alone after desired blood pressure levels are reached with combination medication.

Riker Northridge, California

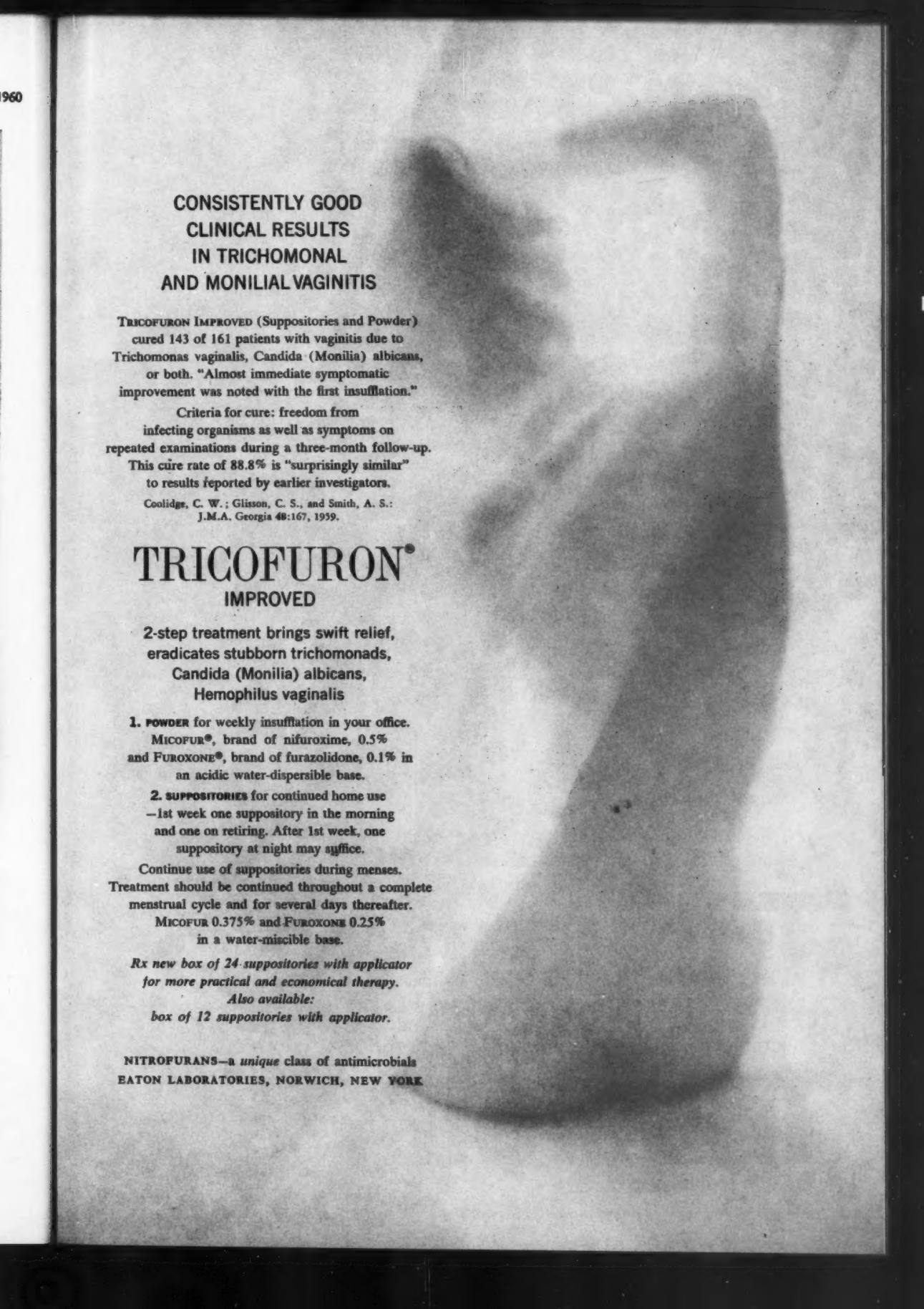
Novahistine® works better than antihistamines alone

Stuffy, runny noses...swollen, weepy eyes are more effectively relieved with Novahistine. The distinctly additive action of the vasoconstrictor and antihistamine combined in Novahistine relieves allergic symptoms more effectively than either drug alone.

One dose of 2 tablets for day-long or night-long relief.
Each long-acting tablet contains 25 mg. phenylephrine HCl and 4 mg. chlorprophenpyridamine maleate.
Bottles of 50 and 250 green, film-coated tablets.

PITMAN-MOORE COMPANY Division of Allied Laboratories, Inc., Indianapolis 6, Indiana

Novahistine LP LONG-ACTING



CONSISTENTLY GOOD CLINICAL RESULTS IN TRICHOMONAL AND MONILIAL VAGINITIS

TRICOFURON IMPROVED (Suppositories and Powder) cured 143 of 161 patients with vaginitis due to Trichomonas vaginalis, Candida (Monilia) albicans, or both. "Almost immediate symptomatic improvement was noted with the first insufflation."

Criteria for cure: freedom from infecting organisms as well as symptoms on repeated examinations during a three-month follow-up. This cure rate of 88.8% is "surprisingly similar" to results reported by earlier investigators.

Coolidge, C. W.; Glisson, C. S., and Smith, A. S.: J.M.A. Georgia 48:167, 1959.

TRICOFURON®

IMPROVED

2-step treatment brings swift relief, eradicates stubborn trichomonads, Candida (Monilia) albicans, Hemophilus vaginalis

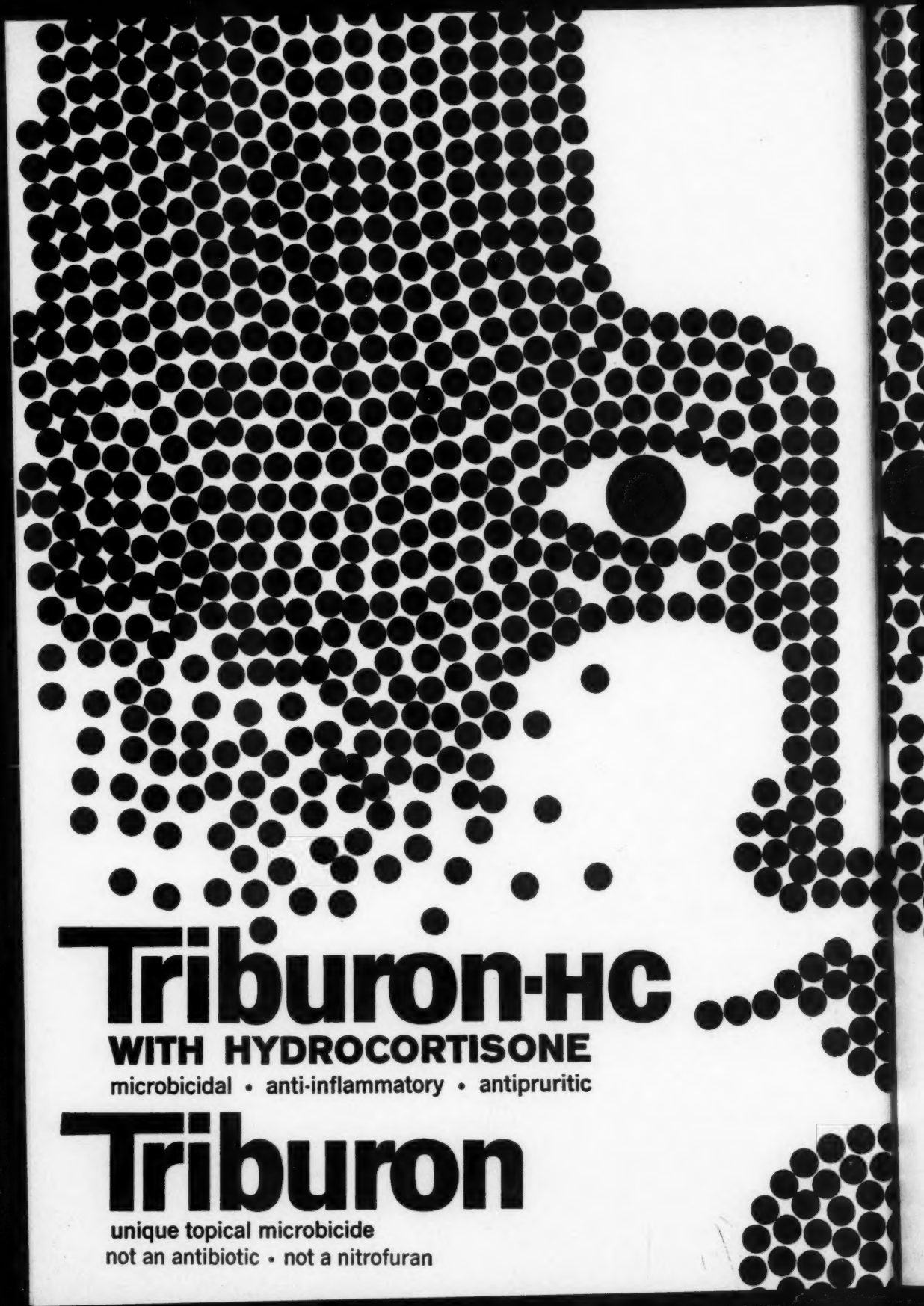
1. POWDER for weekly insufflation in your office. MICOFUR®, brand of nifuroxime, 0.5% and FUROXONE®, brand of furazolidone, 0.1% in an acidic water-dispersible base.

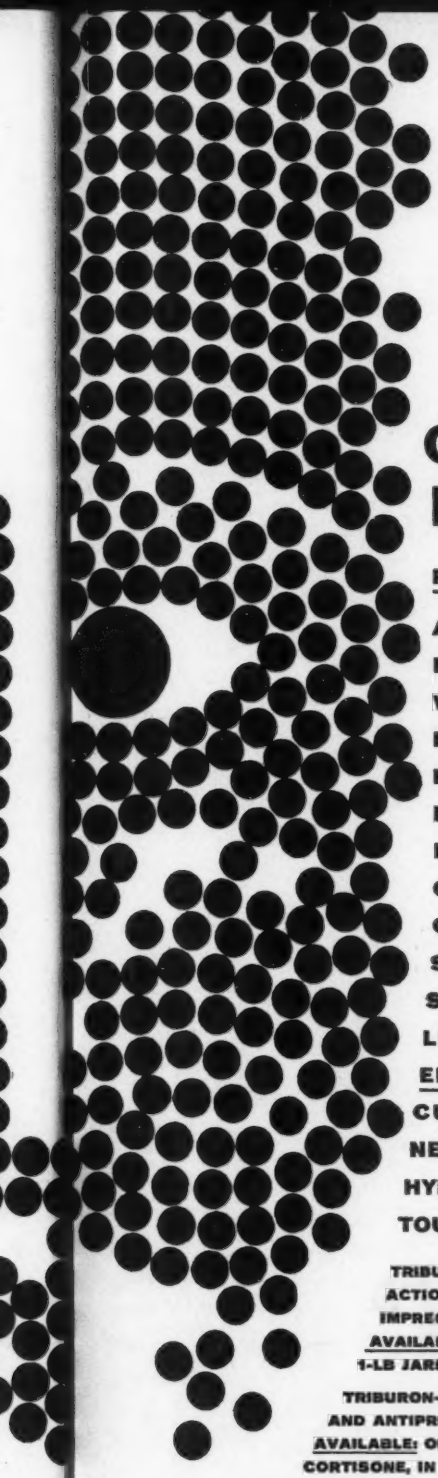
2. SUPPOSITORIES for continued home use —1st week one suppository in the morning and one on retiring. After 1st week, one suppository at night may suffice.

Continue use of suppositories during menses. Treatment should be continued throughout a complete menstrual cycle and for several days thereafter. MICOFUR 0.375% and FUROXONE 0.25% in a water-miscible base.

Rx new box of 24 suppositories with applicator for more practical and economical therapy.
Also available:
box of 12 suppositories with applicator.

NITROFURANS—a *unique* class of antimicrobials
EATON LABORATORIES, NORWICH, NEW YORK


Triburon-HC
WITH HYDROCORTISONE
microbicidal • anti-inflammatory • antipruritic
Triburon
unique topical microbicide
not an antibiotic • not a nitrofuran



CONSISTENT RESPONSE IN SKIN INFECTIONS

REGARDLESS OF VIRULENCE, RESISTANCE, CHRONICITY

A DISTINCTIVE ANTIMICROBIAL, TRIBURON PREVAILS OVER PRIMARY AND SECONDARY INVADERS PROMPTLY, SAFELY, WITH NO SIGNIFICANT LOSS OF ORGANISM SENSITIVITY.[1] TWO FORMS: TRIBURON FOR SKIN AND WOUND INFECTIONS, TRIBURON-HC (WITH HYDROCORTISONE) TO COUNTER ITCHING AND INFLAMMATION AS WELL AS INFECTION. BOTH HAVE ACHIEVED IMPRESSIVE CLINICAL RECORDS:

- **EFFECTIVE IN OVER 90% OF PATIENTS[2-5]**
- **DRAMATIC RESPONSES IN CHRONIC CONDITIONS[4, 6]**
- **MICROBICIDAL EVEN AGAINST RESISTANT STRAINS OF STAPH. AND STREP.[1, 4]**
- **VIRTUALLY NONSENSITIZING AND NONIRRITATING[2-5]**
- **STAINLESS, ODORLESS, "HIGHLY ACCEPTABLE"[5].**

EFFECTIVE THERAPY FOR: IMPETIGO, FOLLICULITIS, FURUNCULOSIS, ECTHYMA, ECZEMA, ACNE, ATOPIC DERMATITIS, NEURODERMATITIS, CONTACT DERMATITIS, STASIS ULCERS, HYDRADENITIS, SEBORRHEIC DERMATITIS, INFECTIOUS ECZEMATOUS DERMATITIS, WOUNDS AND LACERATIONS.

TRIBURON—FOR ALL SKIN AND WOUND INFECTIONS REQUIRING CONSISTENT ANTIBACTERIAL ACTION, AND FOR PREVENTION AND TREATMENT OF POST-BURN INFECTIONS. (TRIBURON-IMPREGNATED DRESSINGS CAN BE AUTOCLAVED.)
AVAILABLE: OINTMENT, CONTAINING 0.1 PER CENT TRIBURON CHLORIDE, IN 1-OZ TUBES AND 1-LB JARS.

TRIBURON-HC—FOR INFLAMMATORY AND ECZEMATOID DERMATOSES WHERE ANTI-INFLAMMATORY AND ANTIPRURITIC BENEFITS AS WELL AS ANTIBACTERIAL EFFECTS ARE REQUIRED.
AVAILABLE: OINTMENT, CONTAINING 0.1 PER CENT TRIBURON CHLORIDE PLUS 0.5 PER CENT HYDROCORTISONE, IN 5-GM AND 20-GM TUBES.

REFERENCES: 1. R. J. SCHNITZER, E. GRUNBERG, W. F. DELORENZO AND R. E. BAGDON, ANTIBIOTICS & CHEMOTHER., 9:267, 1959. 2. R. C. V. ROBINSON, ANN. NEW YORK ACAD. SC., 82:(ART. 1), 144, 1959. 3. E. EDELSON, E. GRUNBERG, A. D. CALABRESE AND T. V. MORTON, IBID., P. 124. 4. P. L. WILLIAMS, IBID., P. 135. 5. F. T. BECKER AND J. L. TUURA, IBID., P. 131. 6. S. M. BLUEFARB, IBID., P. 119.

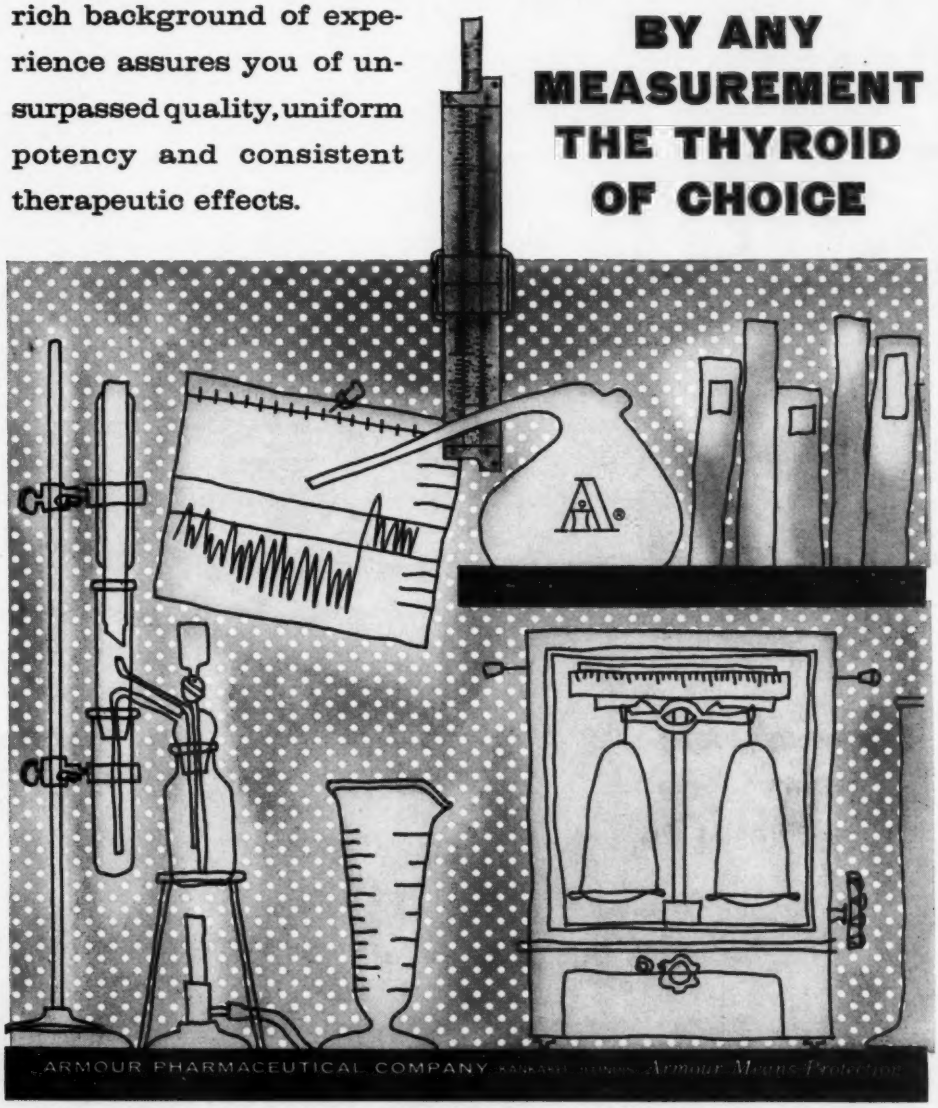
TRIBURON® CHLORIDE — N,N'-BIS[1-METHYL-3-(2,2,6-TRIMETHYLCYCLOHEXYL) PROPYL]-N,N'-DIMETHYL-1,6-HEXANEDIAMINE BIS (METHOCHLORIDE)

ROCHE LABORATORIES • DIVISION OF HOFFMANN-LA ROCHE INC • NUTLEY 10, N. J.

ALWAYS SPECIFY ARMOUR THYROID

ARMOUR THYROID for over half a century has been more widely prescribed...more widely dispensed than any other thyroid product. Pioneer in thyroid standardization, Armour's rich background of experience assures you of unsurpassed quality, uniform potency and consistent therapeutic effects.

BY ANY MEASUREMENT THE THYROID OF CHOICE



she calls it "nervous indigestion"

diagnosis: a wrought-up patient with a functional gastro-intestinal disorder compounded by inadequate digestion. **treatment:** reassurance first, then medication to relieve the gastric symptoms, calm the emotions, and enhance the digestive process. **prescription:** new Donnazyme—providing the multiple actions of widely accepted Donnatal® and Entozyme®—two tablets t.i.d., or as necessary.

Each Donnazyme tablet contains
—In the gastric-soluble outer layer: Hyoscyamine sulfate, 0.0518 mg.; Atropine sulfate, 0.0097 mg.; Hyoscine hydrobromide, 0.0033 mg.; Phenobarbital (1/8 gr.), 8.1 mg.; and Pepsin, N. F., 150 mg. **In the enteric-coated core:** Pancreatin, N. F., 300 mg., and Bile salts, 150 mg.

ANTISPASMODIC - SEDATIVE - DIGESTANT

DONNAZYME®

A. H. ROBINS COMPANY, INCORPORATED • RICHMOND 20, VIRGINIA

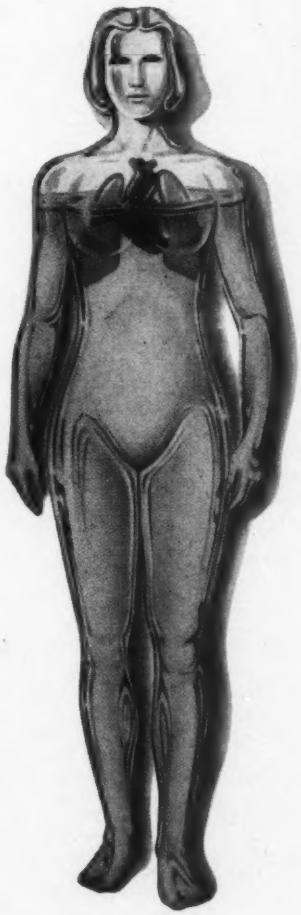
in edema of pregnancy "gratifying relief..." in all patients treated with

HYDRODIURIL®

HYDROCHLOROTHIAZIDE

increased potency–without corresponding increase in side effects

Ford, Ralph V.: Southern Med. Jl. 52: 40, (Jan.) 1959



"Hydrochlorothiazide was given to patients with edema (mild to moderate) of varied etiology..." "There were...5 women in the third trimester of pregnancy." In these patients the cumulative weight loss was 2 pounds after seven days of therapy and 4 pounds after twenty-one days. Gratifying relief of edema was observed in all patients.

DOSAGE: One or two 50 mg. tablets HYDRODIURIL once or twice a day, depending upon the condition and individual patient response.

SUPPLIED: 25 mg. and 50 mg. scored tablets HYDRODIURIL (Hydrochlorothiazide) in bottles of 100 and 1,000.

HYDRODIURIL is a trademark of Merck & Co., INC.

Additional information on HYDRODIURIL is available to the physician on request. ©1960 Merck & Co., INC.

MSD MERCK SHARP & DOHME
Division of Merck & Co., Inc. Philadelphia 1, Pa.

Cartoon idea by pharmacist Emil Magdalener

Many of you may have seen a recent cartoon depicting a midnight scene in front of a pharmacy. A woman is pounding on the door and the pharmacist is leaning out the window of his apartment over the store. "Open up," shouts the woman. "My husband is sick and I need a stamp so I can send this prescription to the mail order house."

The drug that always fails is the drug that isn't there

Far-fetched? Perhaps, but there are those who would have us believe that our present system of drug distribution is inefficient and costly, and should be replaced by presumably more efficient and cheaper centralized or bureaucratic methods. Disregarding the probable political philosophy behind these suggestions, consider what a marvelously intricate and efficient system of drug distribution we have in this country. • From the laboratories of the manufacturers comes a steady stream of new and better drugs for your patients. Warehoused and stocked by drug wholesalers, these products are available in over 53,000 pharmacies scattered across the length and breadth of our land. And woe to the pharmacist who hasn't been provided with yesterday's laboratory discovery for your use in treating a patient today. • The economists speak of "utility of time" and "utility of place." We simply say that you can confidently prescribe *what* you choose, *when* it is needed, *wherever* your patient may be.

This message is brought to you by the producers of prescription drugs as a service to the medical profession. For additional information, please write Pharmaceutical Manufacturers Association, 1411 K Street, N.W., Washington 5, D.C.

When summertime chores bring on **LOW BACK PAIN**

Trancopal®

Brand of chlormezanone

relaxes skeletal muscle spasm—ends disability.

When any of a host of summer activities brings on low back pain associated with skeletal muscle spasm, your patient need not be disabled or even uncomfortable. The spasm can be relaxed with Trancopal, and relief of pain and disability will follow promptly.

Lichtman[1,2] used Trancopal to treat patients with low back pain, stiff neck, bursitis, rheumatoid arthritis, osteoarthritis, trauma, and postoperative muscle spasm. He noted that Trancopal produced satisfactory relief in 817 of 879 patients (excellent results in 268, good in 448 and fair in 101).

Gruenberg[3] prescribed Trancopal for 70 patients with low back pain and observed that it brought marked improvement to all. "In addition to relieving spasm and pain, with subsequent improvement in movement and function, Trancopal reduced restlessness and irritability in a number of patients."[3] In another series, Kearney[4] reported that Trancopal produced relief in 181 of 193 patients suffering from low back pain and other forms of musculoskeletal spasm.

Trancopal enables the anxious patient to work or play. According to Gruenberg, "In addition to relieving muscle spasm in a variety of musculoskeletal and neurologic conditions, Trancopal also exerts a marked tranquilizing action in anxiety and tension states."[3] Kearney[4] found "... that Trancopal is the most effective oral skeletal muscle relaxant and mild tranquilizer currently available."

Side effects are rare and mild. "Trancopal is exceptionally safe for clinical use."[3] In the 70 patients with low back pain treated by Gruenberg,[3] the only side effect noted was mild nausea which occurred in 2 patients. In Lichtman's group, "No patient discontinued chlormethazanone [Trancopal] because of intolerance."[1]

low Supplied: Trancopal Caplets®
200 mg. (green colored, scored), bottles of 100.
100 mg. (peach colored, scored), bottles of 100.

Usage: Adults, 200 or 100 mg. orally three or four mes daily. Relief of symptoms occurs in from fteen to thirty minutes and lasts from four to six ours.

ferences: 1. Lichtman, A. L.: *Kentucky Acad. Gen. act. J.* 4:28, Oct., 1958. 2. Lichtman, A. L.: Scientific Exhibit, Internat. Coll. Surgeons, Miami Beach, Fla., Jan. 3, 1959. 3. Gruenberg, Friedrich: *Current Therap. Res.* 1, Jan., 1960. 4. Kearney, R. D.: *Current Therap. Res.* 127, April, 1960.

Winthrop LABORATORIES
New York 18, N.Y.

Lifts depression... a

You see an improvement within a few days
Thanks to your prompt treatment and the smooth action of Deprol, her depression is relieved and her anxiety and tension calmed – *often in a few days.* She eats well, sleeps well and soon returns to her normal activities.

..as it calms anxiety!

Smooth, balanced action lifts depression as it calms anxiety... rapidly and safely

Balances the mood – no "seesaw" effect of amphetamine-barbiturates and energizers. While amphetamines and energizers may stimulate the patient – *they often aggravate anxiety and tension.*

And although amphetamine-barbiturate combinations may counteract excessive stimulation – *they often deepen depression.*

In contrast to such "seesaw" effects, Deprol's smooth, *balanced* action lifts depression as it calms anxiety – both at the same time.

Acts swiftly – the patient often feels better, sleeps better, within a few days. Unlike the delayed action of most other antidepressant drugs, which may take two to six weeks to bring results, Deprol relieves the patient quickly – often within a few days. Thus, the expense to the patient of long-term drug therapy can be avoided.

Acts safely – no danger of liver damage. Deprol does not produce liver damage, hypotension, psychotic reactions or changes in sexual function – frequently reported with other antidepressant drugs.

Bibliography *(13 clinical studies, 858 patients)*: **1.** Alexander, L. (35 patients): Chemotherapy of depression – Use of meprobamate combined with benactyzine (2-diethylaminoethyl benzilate) hydrochloride. J.A.M.A. 166:1019, March 1, 1958. **2.** Bateman, J. C. and Carlton, H. N. (50 patients): Meprobamate and benactyzine hydrochloride (Deprol) as adjunctive therapy for patients with advanced cancer. Antibiotic Med. & Clin. Therapy 6:648, Nov. 1959. **3.** Beerman, H. M. (44 patients): The treatment of depression with meprobamate and benactyzine hydrochloride. Western Med. 1:10, March 1960. **4.** Bell, J. L., Tauber, H., Santy, A. and Pulito, F. (77 patients): Treatment of depressive states in office practice. Dis. Nerv. System 20:263, June 1959. **5.** Breitner, C. (31 patients): On mental depressions. Dis. Nerv. System 20:142, (Section Two), May 1959. **6.** Gordon, P. E. (50 patients): Deprol in the treatment of depression. Dis. Nerv. System 21:215, April 1960. **7.** Landman, M. E. (50 patients): Clinical trial of a new antidepressive agent. J. M. Soc. New Jersey. In press, 1960. **8.** McClure, C. W., Papas, P. N., Speare, G. S., Palmer, E., Slattery, J. J., Konefal, S. H., Henken, B. S., Wood, C. A. and Ceresia, G. B. (128 patients): Treatment of depression – New technics and therapy. Am. Pract. & Digest Treat. 10:1525, Sept. 1959. **9.** Pennington, V. M. (135 patients): Meprobamate-benactyzine (Deprol) in the treatment of chronic brain syndrome, schizophrenia and senility. J. Am. Geriatrics Soc. 7:656, Aug. 1959. **10.** Rickels, K. and Ewing, J. H. (35 patients): Deprol in depressive conditions. Dis. Nerv. System 20:364, (Section One), Aug. 1959. **11.** Ruchwarger, A. (87 patients): Use of Deprol (meprobamate combined with benactyzine hydrochloride) in the office treatment of depression. M. Ann. District of Columbia 28:438, Aug. 1959. **12.** Settel, E. (52 patients): Treatment of depression in the elderly with a meprobamate-benactyzine hydrochloride combination. Antibiotic Med. & Clin. Therapy 7:28, Jan. 1960. **13.** Splitter, S. R. (84 patients): Treatment of the anxious patient in general practice. J. Clin. & Exper. Psychopath. In press, April-June 1960.

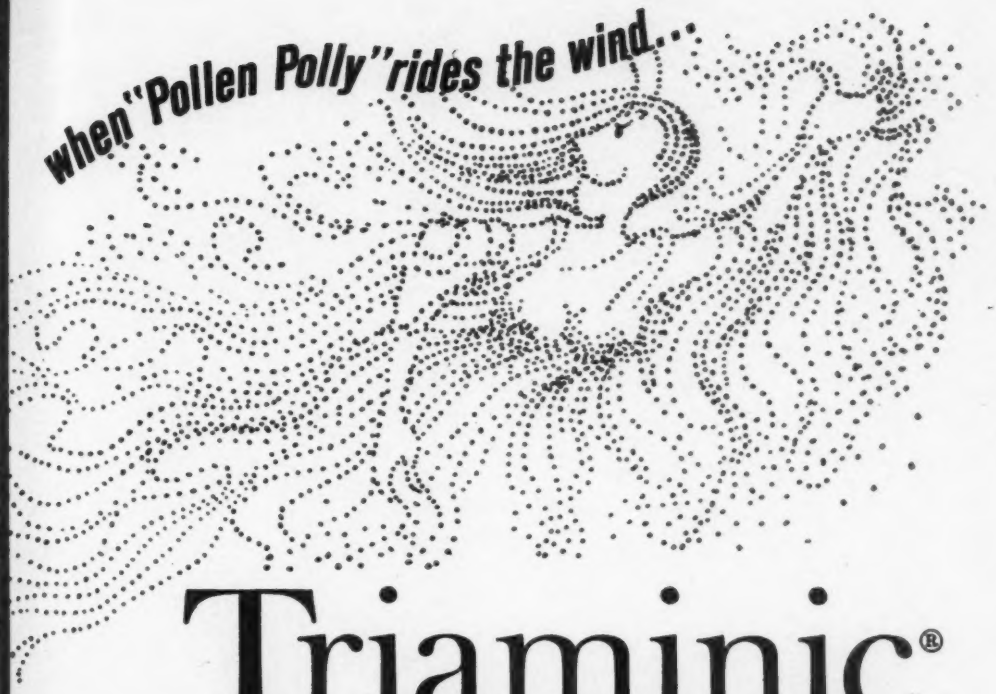
▲Deprol▲

Dosage: Usual starting dose is 1 tablet q.i.d. When necessary, this dose may be gradually increased up to 3 tablets q.i.d.

Composition: 1 mg. 2-diethylaminoethyl benzilate hydrochloride (benactyzine HCl) and 400 mg. meprobamate.
Supplied: Bottles of 50 light-pink, scored tablets. Write for literature and samples.

WALLACE LABORATORIES / *New Brunswick, N. J.*

CD-2127



Triaminic®

...relief from pollen allergies

more complete than antihistamines alone... more thorough than nose drops or sprays

The miseries of respiratory allergy can be relieved so effectively with Triaminic.[1-5] Triaminic contains two antihistamines plus the decongestant, phenylpropanolamine, to help shrink the engorged capillaries, reduce congestion and bring relief from rhinorrhea and sinusitis.[1] Oral administration distributes medication to *all* respiratory membranes without risk of "nose drop addiction" or rebound congestion.[2,3]

Each Triaminic timed-release Tablet provides:

Phenylpropanolamine HCl	50 mg.
Pheniramine maleate	25 mg.
Pyrilamine maleate	25 mg.

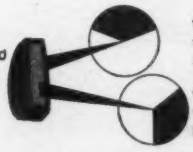
also available:

TRIAMINIC JUVELETS® ½ the formulation of the Triaminic Tablet with timed-release action.

TRIAMINIC SYRUP each teaspoonful (5 ml.) provides ¼ the formulation of the Triaminic Tablet.

References: 1. Fabricant, N. D.: E.E.N.T. Monthly 37:460 (July) 1958. 2. Lhotka, F. M.: Illinois M. J. 112:259 (Dec.) 1957. 3. Farmer, D. F.: Clin. Med. 5:1183 (Sept.) 1958. 4. Fuchs, M.; Bodi, T.; Mallen, S. R.; Hernando, L., and Moyer, J. H.: Antibiotic Med. & Clin. Ther. 7:37 (Jan.) 1960. 5. Halpern, S. R., and Rabinowitz, H.: Ann. Allergy 18:36 (Jan.) 1960.

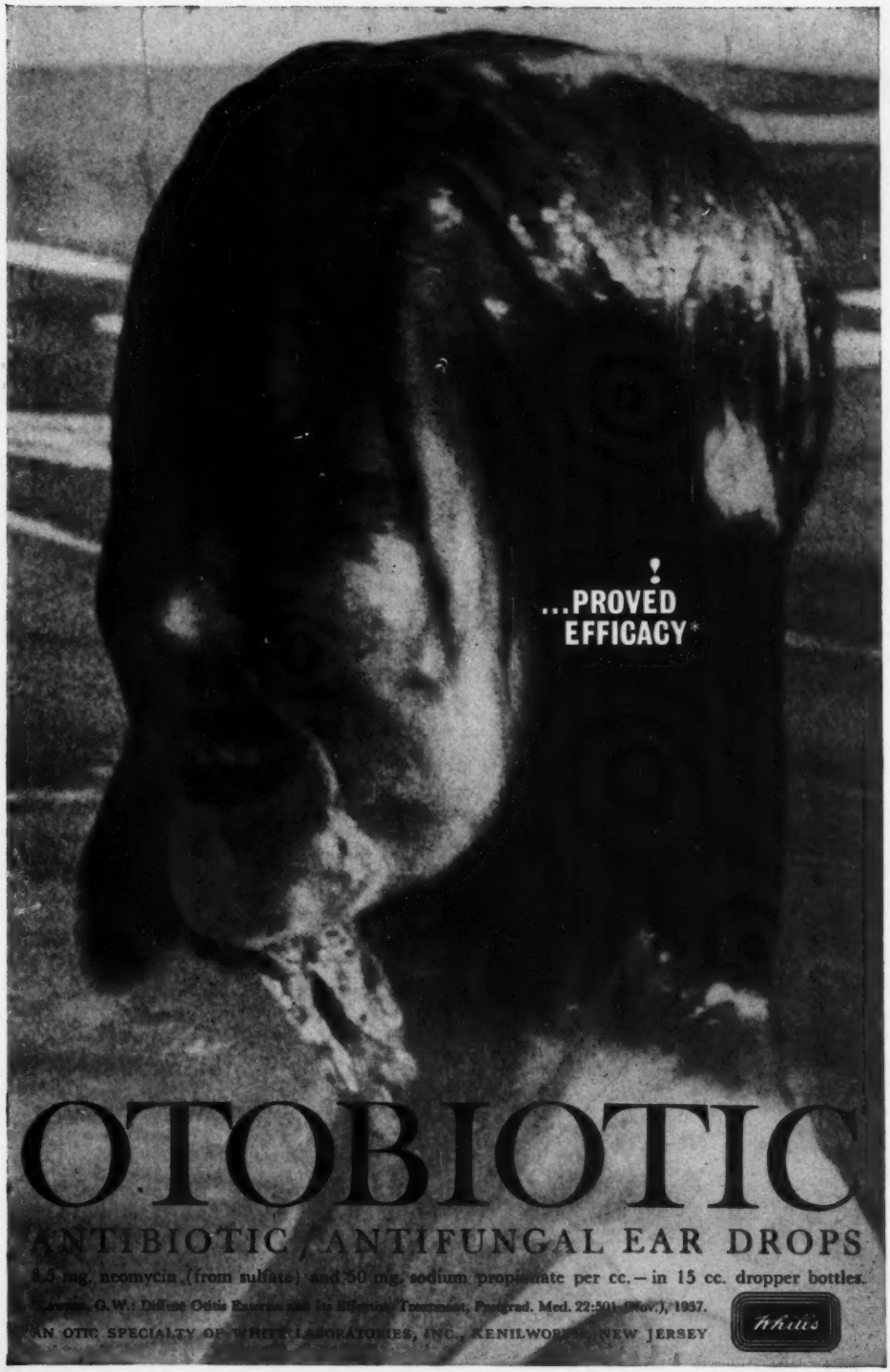
Relief is prompt and prolonged because of this special timed-release action



first—the outer layer dissolves within minutes to produce 3 to 4 hours of relief

then—the core disintegrates to give 3 to 4 more hours of relief

SMITH-DORSEY • A DIVISION OF THE WANDER COMPANY • LINCOLN, NEBRASKA


...PROVED EFFICACY*
OTOBIOTIC
ANTIBIOTIC / ANTIFUNGAL EAR DROPS
3.5 mg. neomycin (from sulfate) and 50 mg. sodium propionate per cc. — in 15 cc. dropper bottles.
Lewis, G.W.: Diffuse Otitis Externa and Its Effective Treatment, Postgrad. Med. 22:501 (Nov.), 1957.
AN OTIC SPECIALTY OF WHITE LABORATORIES, INC., KENILWORTH, NEW JERSEY
Wallis

BUFFERED TO MAINTAIN A NORMAL, LOW pH... LOW SURFACE TENSION FOR THOROUGH CLEANSING OF THE VAGINAL MUCOSA...

Buffers in Massengill Powder solution (pH 3.5 - 4.5) inhibit the neutralizing effect of an alkaline mucosa, maintaining a healthy, low pH for 4 to 6 hours in ambulant patients and up to 24 hours in recumbent patients. This low pH represses the propagation of candida, trichomonas vaginalis, and pathogenic bacteria but permits growth of the beneficial Döderlein bacillus. In contrast, an ordinary, unbuffered douche like vinegar is neutralized within 30 minutes after application. ● Low surface tension of Massengill Powder solution (50 dynes/cm.) enables it to penetrate and cleanse all the folds of the vaginal mucosa more effectively than vinegar (surface tension of 72 dynes/cm.). It also makes cell walls of infecting organisms more susceptible to therapy.

MASSENGILL® POWDER

the buffered acid vaginal douche with low surface tension

THE S. E. MASSENGILL COMPANY Bristol, Tennessee • New York • Kansas City • San Francisco

PATIENTS PREFER

MASSENGILL® POWDER

the buffered acid vaginal douche with low surface tension

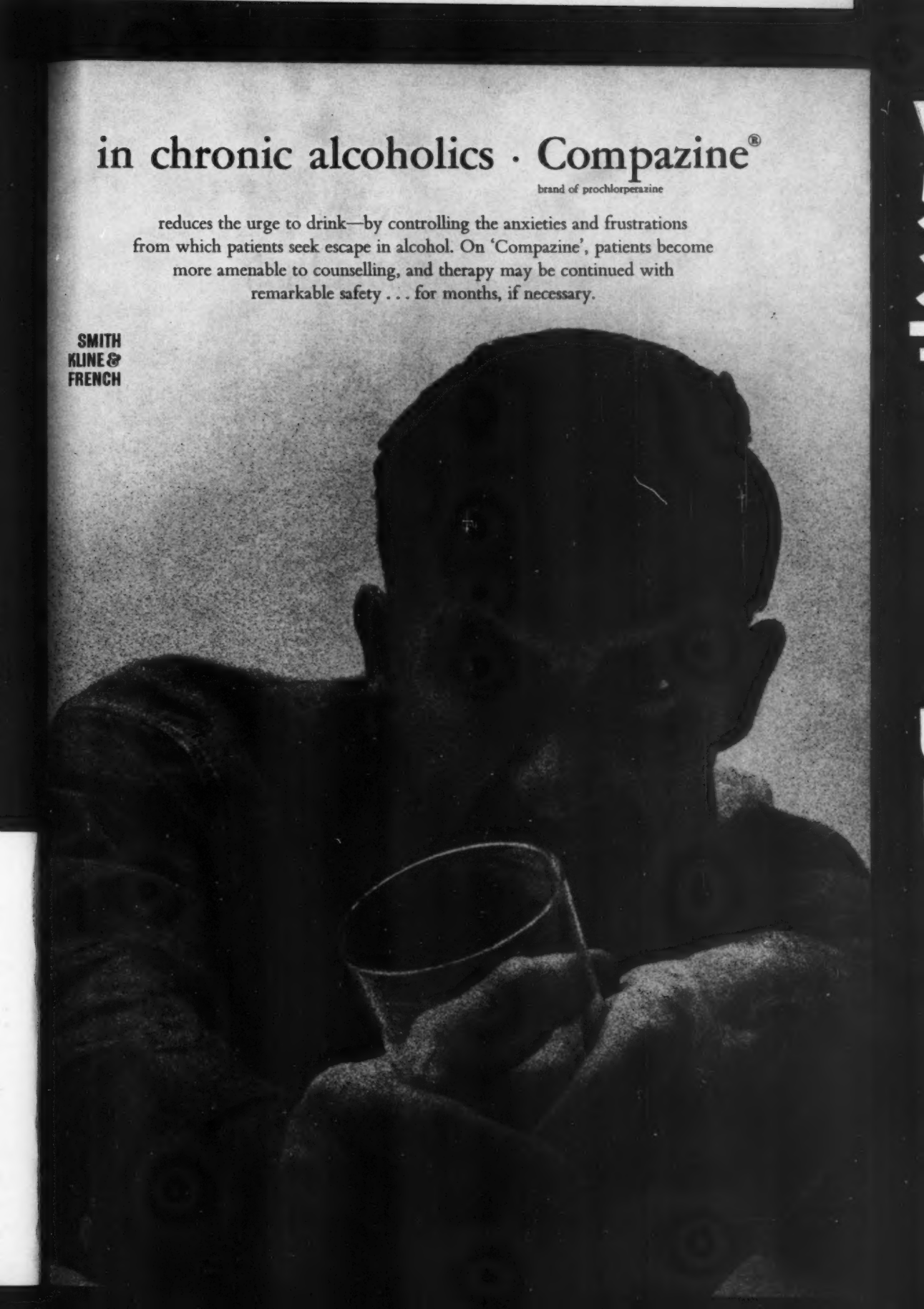
Massengill Powder soothes inflamed tissues, deodorizes, and tends to diminish excessive vaginal secretions. Patients like its clean, refreshing odor.

Massengill Powder is indicated for routine feminine hygiene to guard against infection, and as an adjunct in the management of candida, trichomonas, staphylococcus, and streptococcus vaginal infections.

Contains: Ammonium Alum, Boric Acid, Phenol, Menthol, Berberine, Thymol, Eucalyptol, and Methyl Salicylate. *Write for samples and detailed literature.*

THE S. E. MASSENGILL COMPANY

Bristol, Tennessee • New York • Kansas City • San Francisco


in chronic alcoholics · Compazine®
brand of prochlorperazine
reduces the urge to drink—by controlling the anxieties and frustrations from which patients seek escape in alcohol. On 'Compazine', patients become more amenable to counselling, and therapy may be continued with remarkable safety . . . for months, if necessary.
SMITH KLINE & FRENCH

Fostex® treats their acne while they wash

degreases the skin | helps remove blackheads | dries and peels the skin

completely emulsifies and washes off excess oil from the skin.

penetrates and softens comedones, unblocks pores and facilitates removal of sebum plugs.

removes papule coverings and permits drainage of sebaceous glands.

Patients like Fostex because it is so easy to use. They simply wash acne skin 2 to 4 times a day with Fostex Cream or Fostex Cake, instead of using soap.

Fostex contains Sebulytic®,* a combination of surface-active wetting agents with remarkable antiseborrheic, keratolytic and antibacterial actions . . . enhanced by sulfur 2%, salicylic acid 2%, and hexachlorophene 1%.

*sodium lauryl sulfoacetate, sodium alkyl aryl polyether sulfonate and sodium dioctyl sulfosuccinate.

Fostex is available in two forms—

FOSTEX CREAM, in 4.5 oz. jars.
FOSTEX CAKE, in bar form.

Fostex Cream and Fostex Cake are interchangeable for therapeutic washing of the skin. Fostex Cream is approximately twice as drying as Fostex Cake.

Fostex Cream is also used as a therapeutic shampoo in dandruff and oily scalp.

Write for samples.

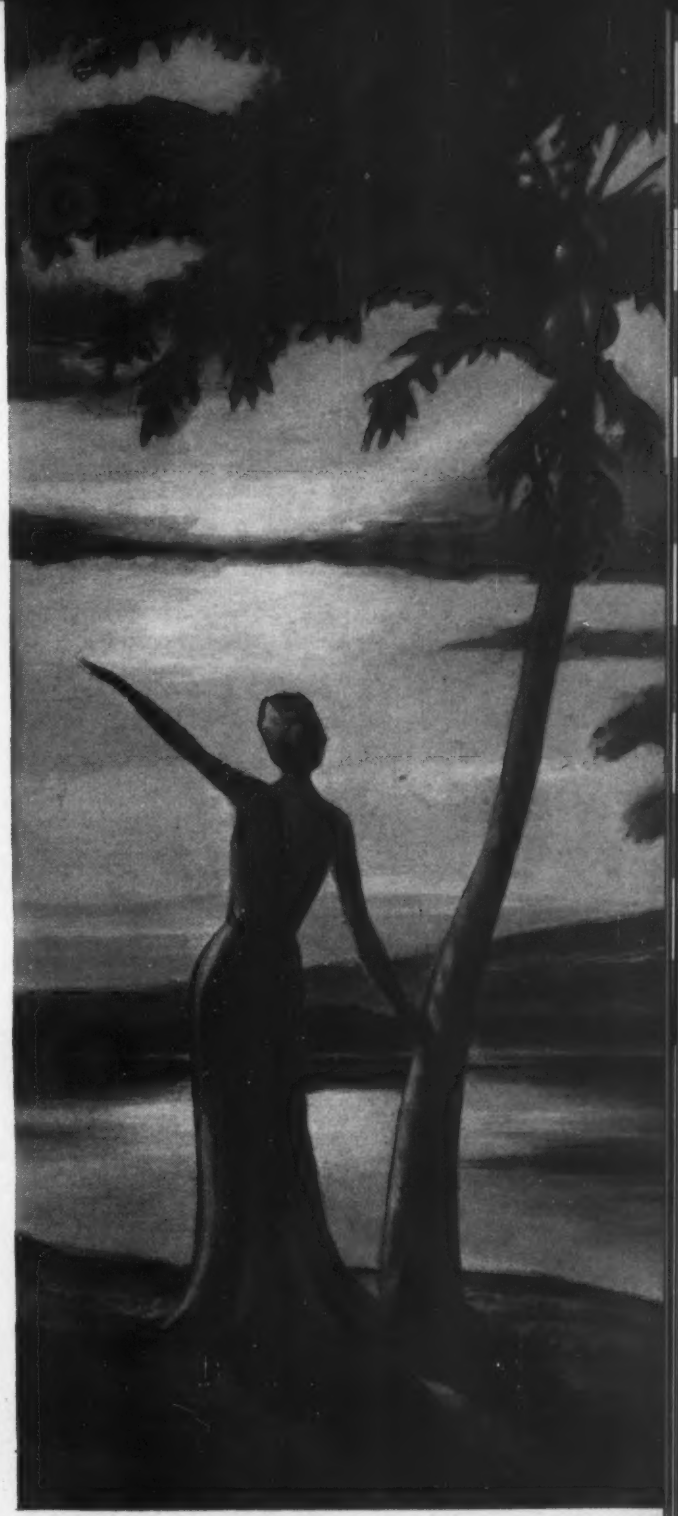
WESTWOOD PHARMACEUTICALS • Buffalo 13, New York

PAPAIN IS THE KEY

to complete, thorough vaginal cleansing

Meta Cine

mucolytic, acidifying, physiologic vaginal douche



The papain content of Meta Cine is the key reason why it effects such complete cleansing of the vaginal vault. Papain is a *natural* digestant, and is capable of rendering soluble from 200-300 times its weight of coagulated egg albumin. In the vagina, papain serves to dissolve mucus plugs and coagulum.

Meta Cine also contains lactose—to promote growth of desirable Doderlein bacilli—and methyl salicylate, eucalyptol, menthol and chlorothymol, to stimulate both circulation and normal protective vaginal secretions. Meta Cine's pleasant, deodorizing, *non-medicinal* fragrance will meet your patients' esthetic demands.

Supplied in 4 oz. and 8 oz. containers, and in boxes of 30 individual-dose packets. Dosage: 2 teaspoonfuls, or contents of 1 packet, in 2 quarts of warm water.

BRAYTEN

BRAYTEN PHARMACEUTICAL COMPANY *Chattanooga 9, Tennessee*

now–for more comprehensive control of *'pain & spasm'*

Robaxi

AHR

ROBAXIN® WITH ASPIRIN

Robins A. H. ROBINS CO., INC., Richmond 20, Virginia

BEFORE: Severe, persistent dermatomycosis of several months duration.

NOW AVAILABLE
WHITE'S VITAMIN
A & D OINTMENT
with **Prednisolone**

AFTER: Same patient after two weeks therapy with Vitamin A and D Ointment with Prednisolone. Medication applied twice daily.

White's Vitamin A and D Ointment is now available **with Prednisolone** (0.5 per cent) in a lanolin-petrolatum base. The local anti-inflammatory and anti-pruritic effects of prednisolone augment the healing, soothing and protective effects of White's Vitamin A and D Ointment. **For dermatoses caused by thermal or chemical irritants, common allergic skin disorders and nonspecific pruritus ani and vulvae.** Supplied in 10 and 25 Gm. tubes.

White Laboratories, Inc., Kenilworth, New Jersey.

by the time you read this 500,000 patients* will have been treated with Altafur®

brand of furaltadone

a "first choice" antimicrobial

In the 10 months since its introduction, ALTAFUR has effected cures in 75 per cent and improvement in an additional 15 per cent of recorded† cases. These cases included:

■ respiratory infections ■ wound infections ■ pyoderma ■ abscess ■ E.E.N.T. infections ■ bacteremia ■ osteomyelitis

Altafur is orally effective against the vast majority of common infections caused by pathogenic bacteria—including antibiotic-resistant staphylococci

■ therapeutic success is outstanding ■ *development of significant bacterial resistance is seldom—if ever—encountered* ■ normal intestinal flora is not unfavorably affected ■ monilial overgrowth has never been reported

For a better index of therapeutic success use Altafur

Tablets of 250 mg. (adult) and 50 mg. (pediatric), bottles of 20 and 100.
Average adult dose: 250 mg. four times a day. Pediatric dosage: 22-25 mg./Kg. (10-11.5 mg./lb.) body weight daily in 4 divided doses. Each dose should be taken with meals, and with food or milk at bedtime. *Alcohol should not be ingested in any form, medicinal or beverage, during* ALTAFUR *therapy and for one week thereafter.*

*Based on a projection of ALTAFUR Tablets dispensed in 10 months since their introduction.

†Compiled by the Medical Department, Eaton Laboratories, from case histories received.

NITROFURANS—a *unique* class of antimicrobials

EATON LABORATORIES, NORWICH, NEW YORK

Proven

in over five years of clinical use and more than 750 published clinical studies

Effective

for relief of anxiety and tension

Outstandingly Safe

- simple dosage schedule produces rapid, reliable tranquilization without unpredictable excitation
- no cumulative effects, thus no need for difficult dosage readjustments
- does not produce ataxia, change in appetite or libido
- does not produce depression, Parkinson-like symptoms, jaundice or agranulocytosis
- does not impair mental efficiency or normal behavior

for the tense and nervous patient

Despite the introduction in recent years of "new and different" tranquilizers, Miltown continues, quietly and steadfastly, to gain in acceptance. Meprobamate (Miltown) is prescribed by the medical profession more than any other tranquilizer in the world.

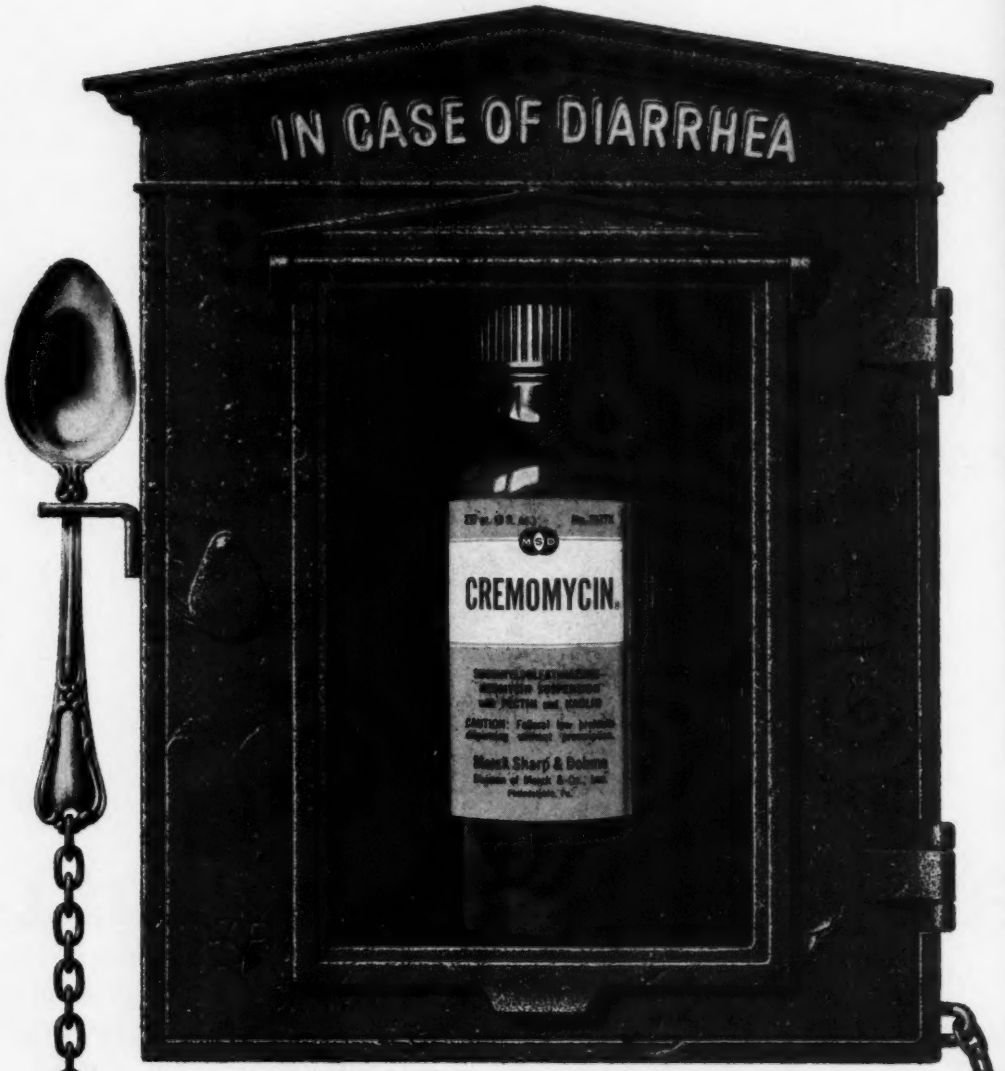
The reasons are not hard to find. Miltown is a ***known*** drug. Its few side effects have been fully reported. ***There are no surprises in store for either the patient or the physician.***

Usual dosage: One or two 400 mg. tablets t.i.d.
Supplied: 400 mg. scored tablets, 200 mg. sugar-coated tablets; or as MEPROTABS*—400 mg. *unmarked*, coated tablets.
*Trade-mark

Miltown®

meprobamate (Wallace)

WALLACE LABORATORIES / *New Brunswick, N. J.*



Cremomycin® provides rapid relief of virtually all diarrheas

NEOMYCIN—rapidly bactericidal against most intestinal pathogens, but relatively ineffective against certain diarrhea-causing organisms.

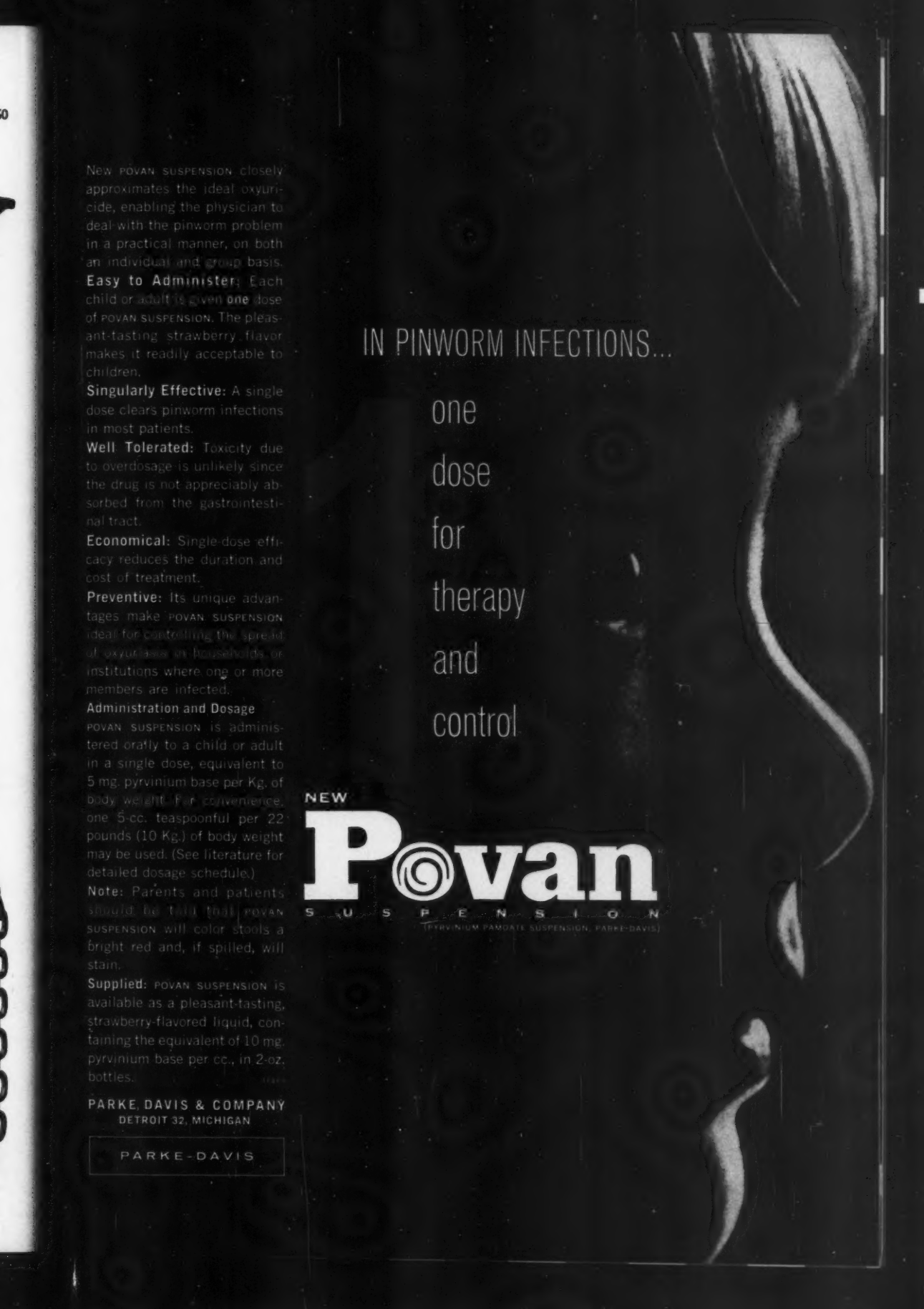
SULFASUXIDINE® (succinylsulfathiazole)—an ideal adjunct to neomycin because it is highly effective against Clostridia and certain other neomycin-resistant organisms.

KAOLIN AND PECTIN—coat and soothe the inflamed mucosa, adsorb toxins, help reduce intestinal hypermotility, help provide rapid symptomatic relief.

For additional information, write Professional Services, Merck Sharp & Dohme, West Point, Pa.

MERCK SHARP & DOHME, DIVISION OF MERCK & CO., Inc., PHILADELPHIA 1, PA.

CREMOMYCIN AND SULFASUXIDINE ARE TRADEMARKS OF MERCK & CO., INC.



New POVAN SUSPENSION closely approximates the ideal oxyuricide, enabling the physician to deal with the pinworm problem in a practical manner, on both an individual and group basis.

Easy to Administer: Each child or adult is given **one** dose of POVAN SUSPENSION. The pleasant-tasting strawberry flavor makes it readily acceptable to children.

Singularly Effective: A single dose clears pinworm infections in most patients.

Well Tolerated: Toxicity due to overdosage is unlikely since the drug is not appreciably absorbed from the gastrointestinal tract.

Economical: Single-dose efficacy reduces the duration and cost of treatment.

Preventive: Its unique advantages make POVAN SUSPENSION ideal for controlling the spread of oxyuriasis in households or institutions where one or more members are infected.

Administration and Dosage

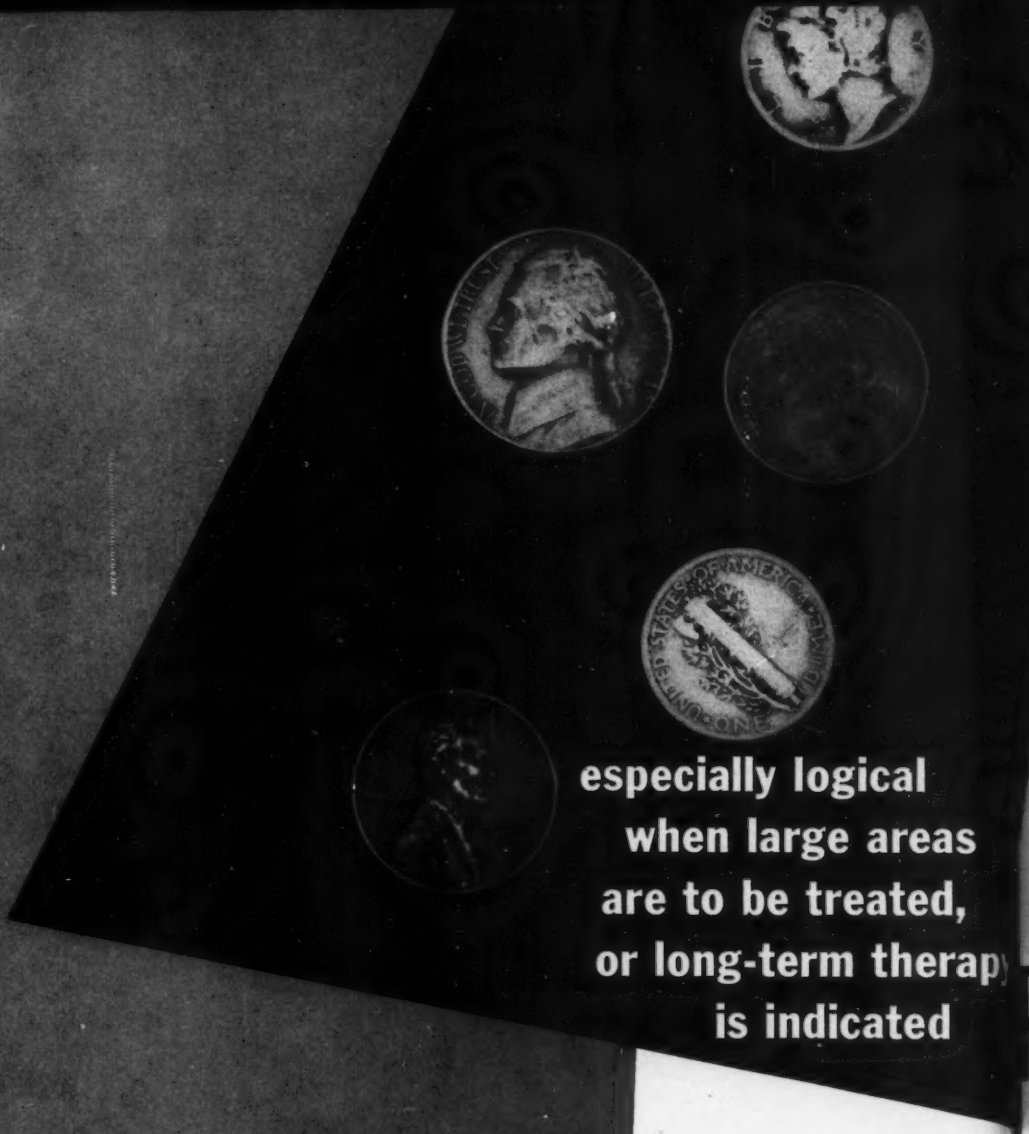
POVAN SUSPENSION is administered orally to a child or adult in a single dose, equivalent to 5 mg. pyrvinium base per Kg. of body weight. For convenience, one 5-cc. teaspoonful per 22 pounds (10 Kg.) of body weight may be used. (See literature for detailed dosage schedule.)

Note: Parents and patients should be told that POVAN SUSPENSION will color stools a bright red and, if spilled, will stain.

Supplied: POVAN SUSPENSION is available as a pleasant-tasting, strawberry-flavored liquid, containing the equivalent of 10 mg. pyrvinium base per cc., in 2-oz. bottles.

PARKE, DAVIS & COMPANY
DETROIT 32, MICHIGAN

PARKE-DAVIS



especially logical when large areas are to be treated, or long-term therapy is indicated

PANTHO-F 0.2% CREAM . . . the dramatic inflammatory-suppressive, antiallergic, antipruritic effects of hydrocortisone

plus the soothing, antipruritic, healing qualities of pantothenylol

promptly alleviate itching, pain, swelling and inflammation, and accelerate healing in . . .

atopic dermatitis (infantile eczemas, allergic eczemas, disseminated neurodermatitis, lichen chronicus simplex, eczematoid dermatitis, etc.)

contact dermatitis (poison ivy, oak, sumac, drugs, cosmetics, metals, chemicals)

effective topical
steroid therapy

no longer expensive!

for the itching,
inflamed skin

PANTHO-F 0.2% CREAM

pruritic lesions
(intractable pruritus, pruritus ani, pruritus vulvae, senile vulvitis)

seborrheic dermatitis

lichenified eczemas

stasis dermatitis

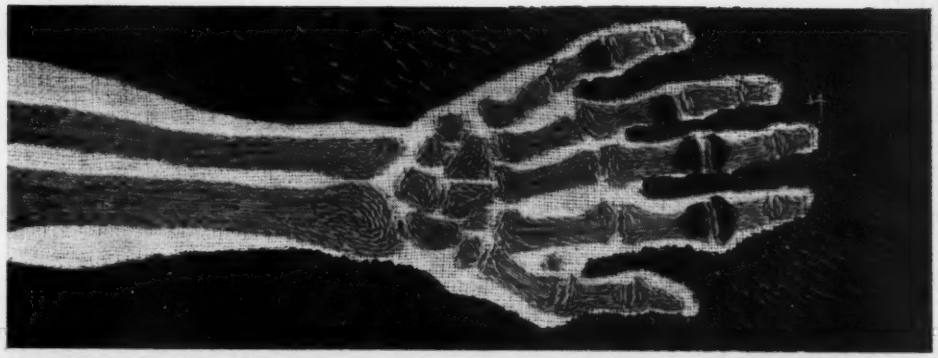
PANTHO-F 0.2% cream provides:	
HYDROCORTISONE*	**0.2%**
PANTOTHENYLOL	**2%**

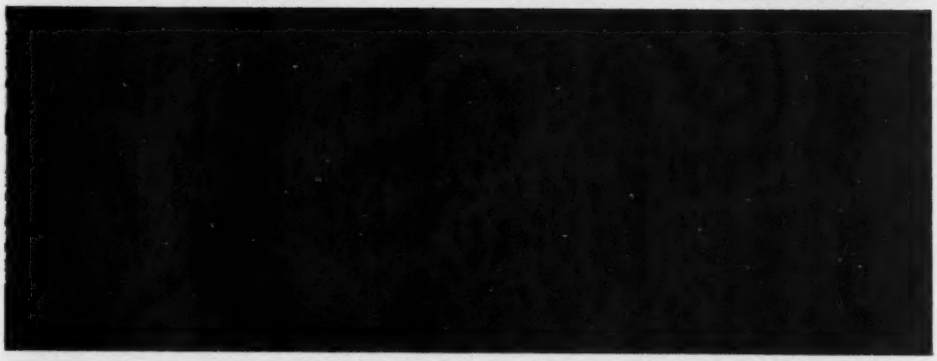
in a stable, water-miscible cream base
*2 mg. hydrocortisone per Gm.

Available in 15 Gm.
and 2 oz. tubes; 1 lb. jars

u. s. vitamin corporation • **PHARMACEUTICALS**
(Arlington-Funk Laboratories, division) • 250 East 43rd Street, New York 17, N. Y.

a promise fulfilled





All corticosteroids provide symptomatic control in rheumatoid arthritis, inflammatory dermatoses, and bronchial asthma. They *differ* in the frequency and severity of side effects. Introduced in 1958, ARISTOCORT Triamcinolone bore the promise of high efficacy and relative safety. Physicians today recognize that the promise has been fulfilled . . . as evidenced by the high rate of refilled ARISTOCORT prescriptions.

Aristocort Triamcinolone LEDERLE

Lederle LEDERLE LABORATORIES, A Division of AMERICAN CYANAMID COMPANY, Pearl River, N.Y.

IN UROPATHIES

WHEN PAIN IS PART OF THE PICTURE

Urinary tract pain, at the source or referred, is subject to the rapid analgesic action of the azo dye in Azo Gantrisin. Azo Gantrisin combines dramatic relief of symptoms with proven effective action against infections carried by either blood stream or urine.

Valuable also following urologic manipulation and surgery.

AZO GANTRISIN

GANTRISIN®—brand of sulfisoxazole ROCHE®

Diagram correlates sources of primary urinary pain with areas of referred pain.

Dosage: Adults—2 tablets four times daily.
Children under 100 lbs—1 tablet four times daily.
Each tablet provides 0.5 Gm Gantrisin plus 50 mg phenylazodiamino-pyridine HCl—bottles of 100 and 500.

ROCHE
LABORATORIES
Division of Hoffmann-La Roche Inc.
Nutley 10, N. J.

Nonsurgical treatment of Endometriosis with

ENOVID®

Seventeen patients[1] with presumed endometriosis selected for pseudopregnancy treatment were given Enovid on a "schedule of 10 mg. daily for ten days, 20 mg. daily for two weeks, and 30 mg. daily thereafter." Treatment was continued for fourteen to twenty weeks.

"They all experienced diminution or elimination of pain during treatment. Nine were entirely free of pain. Others were definitely improved but had occasional episodes of pelvic discomfort. . . . The improvement observed during treatment has generally persisted [during an average follow-up period of five months]. . . . Patients with the most extensive tenderness, nodularity, and symptoms had the best results."

The effect of Enovid in another study is described[2] as follows:

> "Enovid is a potent, orally effective progestin. The addition of 3-methyl ether of ethynylestradiol prevents 'breakthrough' bleeding and produces an ideal mimic of the hormonal changes of pregnancy. Enovid inhibits ovulation, induces a secretory endometrium and produces a decidual effect in areas of endometriosis. It is postulated that, after five to six months of such treatment, decidual necrosis occurs and is followed by gradual absorption."

The author[2] recommends that this therapy be continued for a minimum of five to six months if the pseudopregnancy is being effected to avoid operation. The side effect of nausea, which usually disappears within four or five days, may be diminished by starting with 5 mg. instead of 10 mg. of Enovid, by use of an antiemetic or by administering the drug with the evening meal or with milk or an antacid.

How Supplied: Enovid (brand of norethynodrel with ethynylestradiol 3-methyl ether) is supplied as uncoated, scored, coral-colored tablets of 10 mg. each.

G. D. SEARLE & CO.
CHICAGO 80, ILLINOIS

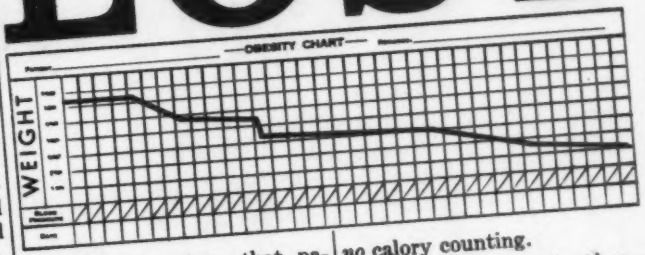
Research in the Service of Medicine

1. Andrews, M. C.; Andrews, W. C., and Strauss, A. F.: Effects of Progestin-Induced Pseudopregnancy on Endometriosis: Clinical and Microscopic Studies, Am. J. Obst. & Gynec. 78:776 (Oct.) 1959.
2. Kistner, R. W.: Endometriosis and Infertility, Clin. Obst. & Gynec. 2:877 (Sept.) 1959.

Journal
E PAPER
ER 25, 1960
FINAL
CITY EDITION
FIVE CENTS

ctory
oned
xpert
reliability
ll out re-
cification,
antee the
extremely
onstration
ed under
m is far
reliability
a.
quipment
simplified
time be-
fter initial
ected and
ilure rate.
the final
But since
onomically
etermined
ture. For
er joints
approxi
on how
hipment,
kelihood
be more
time. An
ilures than
e of serv-
ely trained
rt of the
e files of
o specify
pertinent
ests that
must be
erienced
d cannot
here tests
ty of per-
equipment
ngineering

9,000 TONS OF EXCESS WEIGHT LOST



Case histories show that patients lose an average of 6 lbs. per 100 tablets of Obedrin—making a total weight loss of 18,000,000 lbs. since Obedrin was introduced.

Obedrin and the 60-10-70 Basic Plan succeed where other reducing regimens fail. The Obedrin Basic Plan provides three essentials for weight reduction:

1. Supervision by the physician—Patients need the emotional support and discipline that only the physician can contribute.

2. A balanced eating plan—The 60-10-70 Basic Plan offers the patient a wide variety of menus, carefully calculated to supply a minimum of 60 grams of carbohydrate, 10 grams of fat, and 70 grams of protein each day, with *no* calory counting.

3. Supportive medication—Each capsule or tablet of Obedrin provides:

- Semoxydrine® HCl (methamphetamine HCl), 5 mg., for its anorexigenic and mood-lifting effects
- Pentobarbital, 20 mg., to guard against excitation
- Thiamine Mononitrate, 0.5 mg., Riboflavin, 1 mg., and Nicotinic Acid (Niacin), 5 mg., to supplement the diet
- Ascorbic Acid, 100 mg., to help mobilize tissue fluids

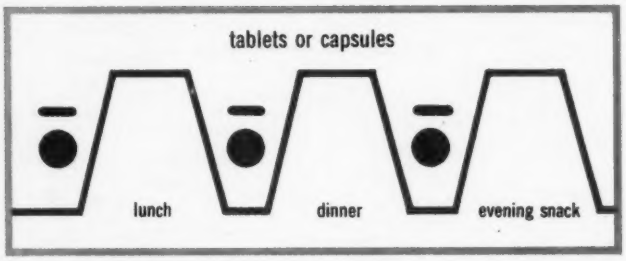
Obedrin and the 60-10-70 Basic Plan help the overweight patient establish correct eating habits... first, to lose excess pounds and then, more important, to *maintain* optimum weight.

Obedrin®

and the 60-10-70 Basic Plan
provide an effective weight-control regimen

THE S. E. MASSENGILL COMPANY
Bristol, Tennessee
New York • Kansas City • San Francisco

A FLEXIBLE DOSAGE FORM PROVIDES DEPENDABLE CONTROL OF APPETITE



The Obedrin formula permits a flexible dosage schedule to depress the appetite at peak hunger periods. The physician can adjust dosage to fit each patient's need.

ADVANTAGES OF OBEDRIN—

A dependable anorexigenic agent
A flexible dosage form
Minimal central nervous stimulation
Vitamins to supplement the diet

Supplied: In bottles of 100, 500, and 1,000

Write for 60-10-70 Basic Plan menus and weight charts.

Obedrin®

and the 60-10-70 Basic Plan

THE S. E. MASSENGILL COMPANY Bristol, Tennessee • New York • Kansas City • San Francisco

NEW

isoclor

provides both . . . / upper respiratory decongestion and bronchial decongestion

Many hay fever patients also experience chest discomfort. For these patients, new ISOCLOR provides relief along the entire respiratory tract.

COMBINES the nasal and bronchial decongestant action of d-isoephedrine with the histamine blocking action of chlorpheniramine.

RELIEVES the discomforts of rhinorrhea, itching, sneezing, hyperlacrimation and post nasal drip—lets the patient get a full night's rest—with minimal daytime drowsiness, CNS or pressor stimulation.

TABLETS AND SYRUP for adults and children . . .

COMPOSITION:	Per tablet	Per 5 ml. syrup
Chlorpheniramine maleate	4 mg.	2 mg.
d-Isoephedrine HCl	25 mg.	12.5 mg.

DOSE: Tablets: One tablet 3 or 4 times daily. Syrup: Children: 3-6 yrs. ½ tsp. t.i.d.; 6-12 yrs. 1 tsp. t.i.d.; Adults: 2 tsp. t.i.d.

AVAILABLE: Tablets: Bottles of 100. Syrup: Pint bottles.

ARNAR-STONE
Laboratories, Inc.
Mt. Prospect, Illinois

Raise the Pain Threshold

WITH MAXIMUM SAFE ANALGESIA

Three Strengths —

PHENAPHEN NO. 2
Phenaphen with Codeine Phosphate ¼ gr. (16.2 mg.)

PHENAPHEN NO. 3
Phenaphen with Codeine Phosphate ½ gr. (32.4 mg.)

PHENAPHEN NO. 4
Phenaphen with Codeine Phosphate 1 gr. (64.8 mg.)

Also —

PHENAPHEN In each capsule

Acetylsalicylic Acid 2½ gr. . (162 mg.)
Phenacetin 3 gr. . . . . (194 mg.)
Phenobarbital ¼ gr. . . . . (16.2 mg.)
Hyoscyamine sulfate . . . . . (0.031 mg.)

PHENAPHEN WITH CODEINE

Robins

Robins

A. H. ROBINS CO., INC., RICHMOND 20, VIRGINIA

Ethical Pharmaceuticals of Merit since 1878

SPEED DURATION

IN *ORAL* CONTROL OF PAIN

ACTS FASTER—usually within 5-15 minutes. **LASTS LONGER**—usually 6 hours or more. **MORE THOROUGH RELIEF**—permits uninterrupted sleep through the night. **RARELY CONSTIPATES**—excellent for chronic or bedridden patients.

AVERAGE ADULT DOSE: 1 tablet every 6 hours. May be habit-forming. Federal law permits oral prescription.

Each PERCODAN® Tablet contains 4.50 mg. dihydrohydroxycodeinone hydrochloride, 0.38 mg. dihydrohydroxycodeinone terephthalate, 0.38 mg. homatropine terephthalate, 224 mg. acetylsalicylic acid, 160 mg. phenacetin, and 32 mg. caffeine.

Also available—for greater flexibility in dosage—PERCODAN®-DEMI: The PERCODAN formula with one-half the amount of salts of dihydrohydroxycodeinone and homatropine.

Endo

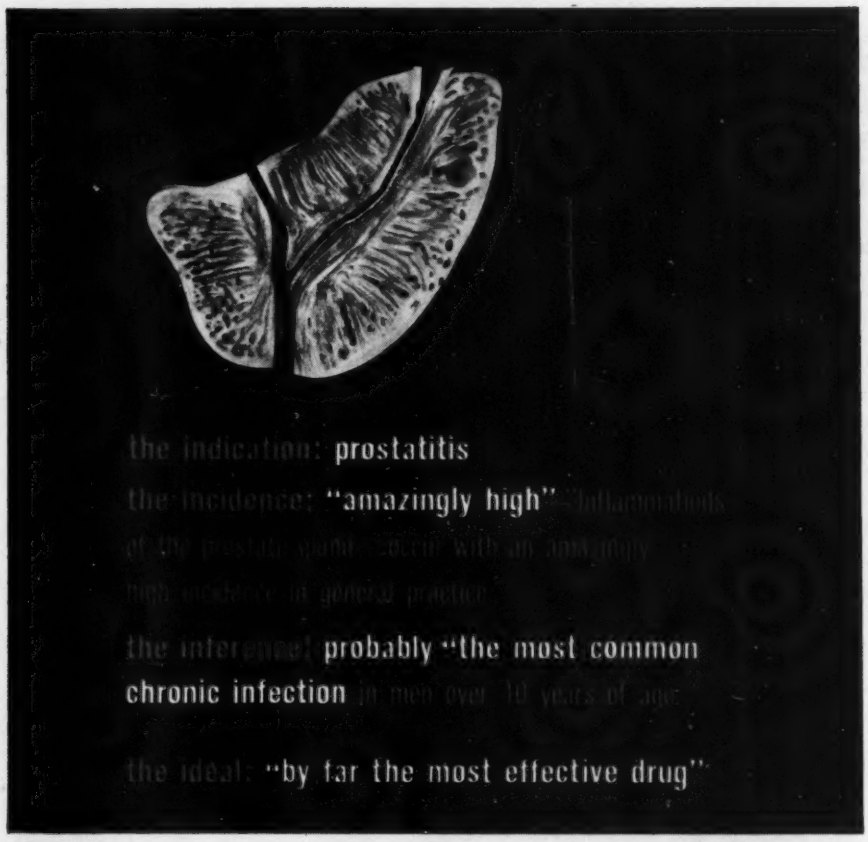
Literature? Write
ENDO LABORATORIES
Richmond Hill 18, New York

Percodan®

salts of Dihydrohydroxycodeinone and Homatropine, plus APC

FOR PAIN

*U.S. Pat. 2,628,185


the indication: prostatitis
the incidence: "amazingly high"
the infectious: probably "the most common chronic infection
the ideal: "by far the most effective drug"

Furadantin®

brand of nitrofurantoin

"... by far the most effective drug to be employed, and this has been substantiated in practice. It is a drug of low toxicity and, what is more important, bacteria rarely if ever become resistant to it. It can be employed for long periods of time, is bactericidal and does not favor the appearance of monilial infections."[3]

Indicated in: acute and chronic prostatitis ■ benign prostatic hypertrophy (to prevent or treat concomitant infection) ■ postoperatively in prostatic surgery

Supplied: Tablets, 50 and 100 mg., Oral Suspension, 25 mg. per 5 cc. tsp.

References: 1. Campbell, M. F.: Principles of Urology, Philadelphia, W. B. Saunders Co., 1957. 2. Farman, F., and McDonald, D. F.: Brit. J. Urol. **31**:176, 1959. 3. Sanjurjo, L. A.: Med. Clin. N. America **43**:1601, 1959.

Eaton®

EATON LABORATORIES, NORWICH, NEW YORK

ANOTHER NOTCH FOR AMPLUS® IMPROVED

(D-AMPHETAMINE + ATARAX® + VITAMINS AND MINERALS)

(AND SHE'S LOSING NOTHING BUT WEIGHT)

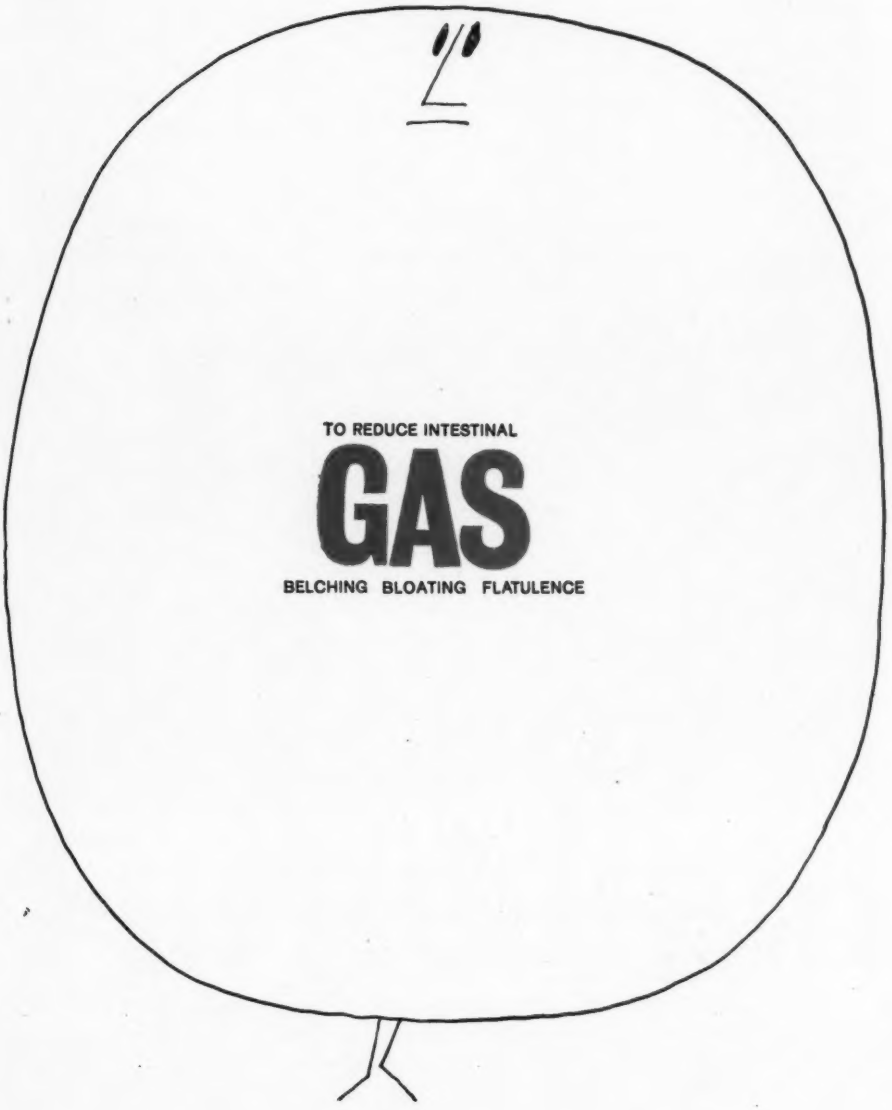
- She's *not* losing her ambition to reduce. (Thanks to d-amphetamine's proven anorectic action.)
- She's *not* losing her composure. (The tranquilizer, Atarax, calms diet-induced anxiety and jitters.)
- She's *not* losing essential vitamins and minerals. (AMPLUS IMPROVED supplies them.)

MAKE THE ONE FOR GOOD MEASURE AMPLUS IMPROVED

One capsule half-hour before each meal. Bottles of 100 soft, soluble capsules, this actual size. Prescription only.

Rx ROERIG

New York 17, N. Y.
Division, Chas. Pfizer & Co., Inc.
Science for the World's Well-Being



A biochemical compound used to diminish intestinal gas in healthy persons and those patients having digestive disorders

KANULASE

Each Kanulase tablet contains Dorase,® 320 units, combined with pepsin, N.F., 150 mg.; glutamic acid HCl, 200 mg.; pancreatin, N.F., 500 mg.; oxbile extract, 100 mg. Dosage: 1 or 2 tablets at mealtime. Supplied: Bottles of 50 tablets.

®DORSEY BRAND OF CELLULASE, EXPRESSED AS DIGESTIVE ACTIVITY UNITS

SMITH-DORSEY • a division of The Wander Company • Lincoln, Nebraska

FREQUENTLY INDICATED FOLLOWING ACCIDENTS

PARAFLEX® FOR RELIEF OF PAINFUL MUSCLE SPASM

Chlorzoxazone®

When accidents result in sprains or strains, PARAFLEX reduces painful spasm promptly. Effective in a wide variety of rheumatic, arthritic and orthopedic disorders, PARAFLEX relieves pain, improves mobility and facilitates rehabilitation. Side effects seldom occur and are rarely severe enough to require discontinuation of therapy. □ *Average Dosage:* Two tablets t.i.d. or q.i.d. □ *Supplied:* Tablets, scored, orange, bottles of 50. Each tablet contains PARAFLEX, 250 mg.

McNEIL

•U.S. Patent No. 2,895,877

McNEIL LABORATORIES, INC · PHILADELPHIA 32, PA.

315A60

REPORTS IN HUNDREDS OF LEADING JOURNALS AND SCORES OF STANDARD TEXTBOOKS REFLECT THE POSITION OF GANTRISIN AS A DRUG OF CHOICE IN GENITOURINARY INFECTIONS: PYELONEPHRITIS/CYSTITIS/PROSTATITIS URETHRITIS/PUERPERAL INFECTIONS

Gantrisin

brand of sulfisoxazole

THE RELIABLE,
HIGHLY SOLUBLE SULFONAMIDE
COVERS THE PREDOMINANT PATHOGENS
ASSURES SAFETY
PROVIDES ROUTINE PROPHYLAXIS

ROCHE LABORATORIES *Division of Hoffmann-La Roche Inc.*

important new therapy in Peptic Ulcer

cessation of all symptoms and complete healing in 70 out of 78 cases as reported in Postgraduate Medicine (Oct.) 1959

"...chymotrypsin offers a new approach to the treatment of peptic ulcer."

In 54 cases, most of them hospitalized, in which chymotrypsin (Chymar) was used in conjunction with other agents "All of the symptoms disappeared and *complete healing of* the ulcer occurred in 49 (90.7 per cent) of the 54 cases . . . " Average time for cessation of symptoms . . . 6 days; for complete healing . . 36 days; average follow-up period . . . 12 months. *In 24 cases* in which Chymar was used alone, "Cessation of all symptoms and *complete healing occurred in 21 (87.5 per cent)* of the 24 cases . . ." Average time for cessation of symptoms . . . 5.8 days; for complete healing . . . 24 days; average follow-up period . . . 25.5 months.

Conclusions: "Because of the excellent results obtained in 78 cases of peptic ulcer . . . I strongly recommend its use as a most valuable adjunct in the treatment of this disease."*

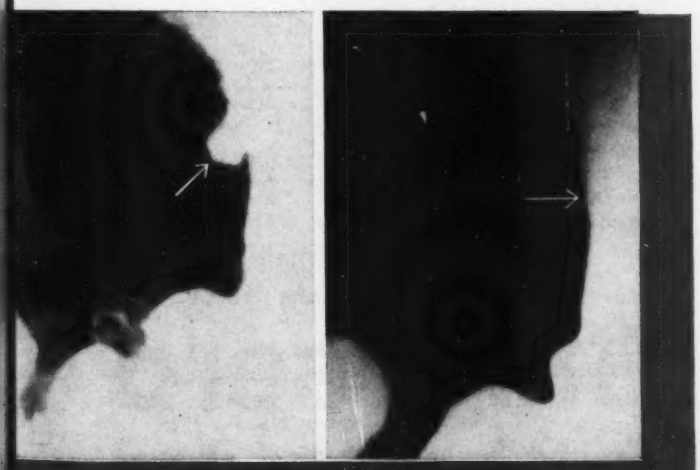
*Mozan, A. A.: Postgraduate Med. 26:542, 1959

the superior anti-inflammatory enzyme

Chymar®

chymotrypsin *Buccal/Aqueous/Oil*

controls inflammation, swelling and pain



Roentgenogram made on January 23, 1957 shows only a slight impression on the lesser curvature.

CHYMAR Buccal—Crystallized chymotrypsin in a tablet formulated for buccal absorption. Bottles of 24 tablets. Enzymatic activity, 10,000 Armour Units per tablet.

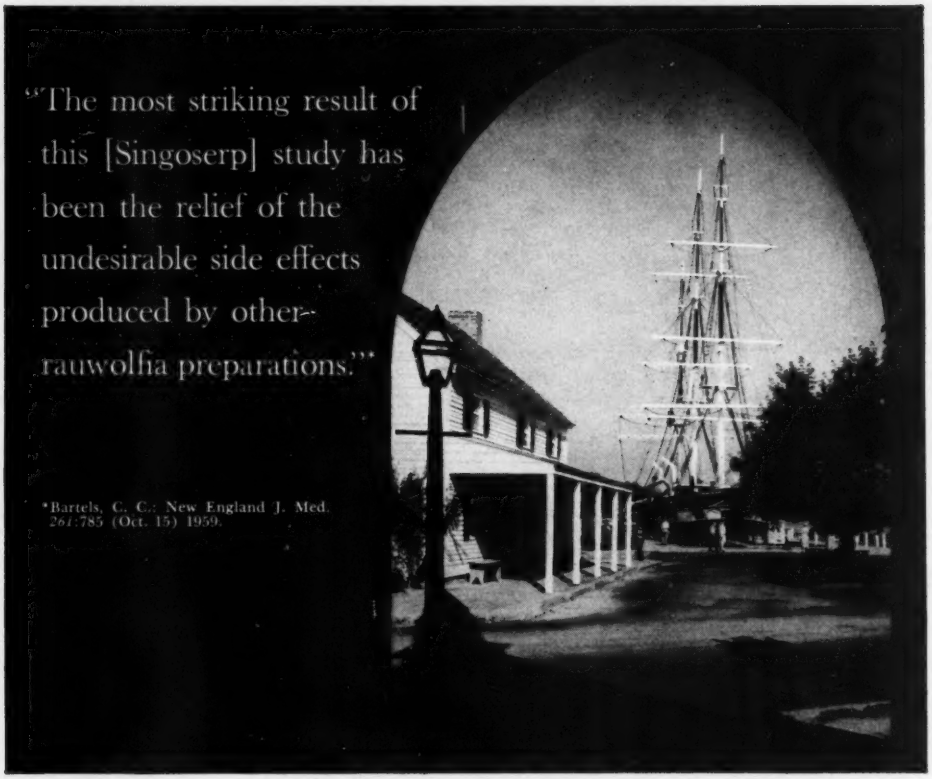
CHYMAR Aqueous—Solution of crystallized chymotrypsin in sodium chloride injection for intramuscular use. Vials of 5 cc. Enzymatic activity, 5000 Armour Units per cc.

CHYMAR—Suspension of crystallized chymotrypsin in oil for intramuscular injection. Vials of 5 cc. Enzymatic activity, 5000 Armour Units per cc.

ARMOUR PHARMACEUTICAL COMPANY
KANKAKEE, ILLINOIS
Armour Means Protection

© 1960, A. P. Co.

from the New England Journal of Medicine:


"The most striking result of this [Singoserp] study has been the relief of the undesirable side effects produced by other rauwolfia preparations."
*Bartels, C. C.: New England J. Med. 261:785 (Oct. 15) 1959.

results you can confirm in your practice:

"In 24 cases syrosingopine was substituted for the rauwolfia product because of 26 troublesome side effects; these symptoms were relieved in all but 3 patients."*

Side Effects	Incidence with Prior Rauwolfia Agent	Incidence with Singoserp
Depression	11	1
Lethargy or fatigue	5	0
Nasal congestion	7	0
Gastrointestinal disturbances	2	2
Conjunctivitis	1	0

(Adapted from Bartels*)

many hypertensive patients prefer

Singoserp®

(syrosingopine CIBA)

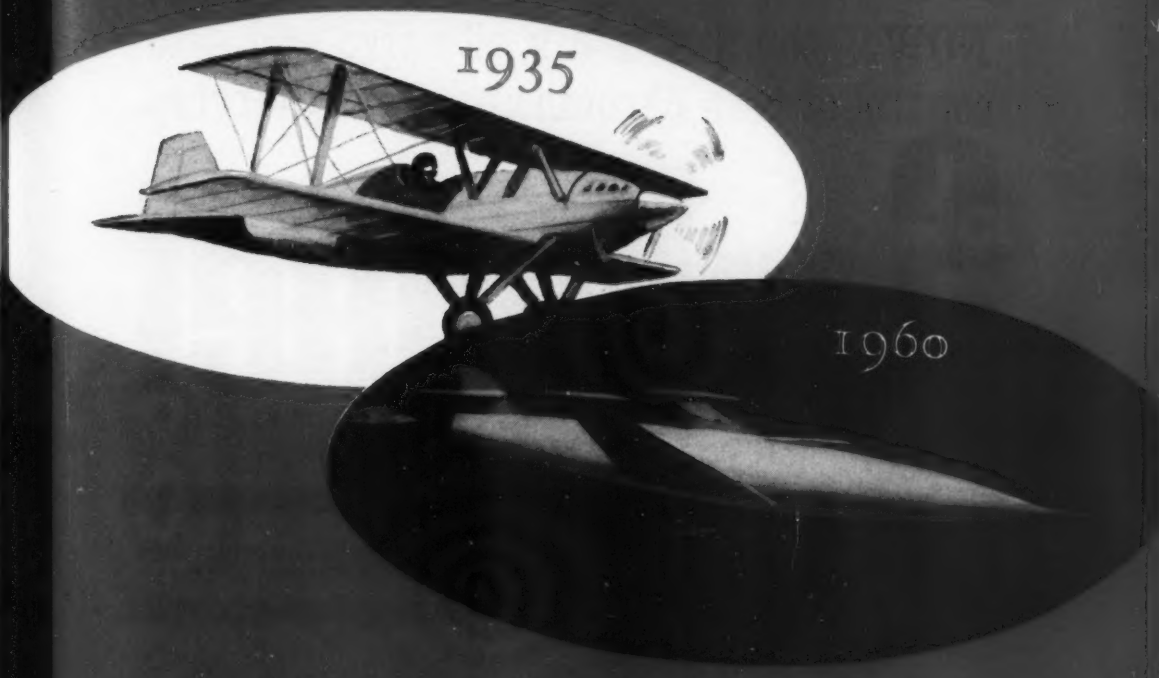
because it lowers their blood pressure without rauwolfia side effects

Tablets, 1 mg. (white, scored); bottles of 100.

Complete information available on request.

CIBA
SUMMIT, NEW JERSEY

Throughout these changing times



Barbidonna®

(PHENOBARBITAL AND NATURAL BELLADONNA ALKALOIDS)

has remained a prescription of choice in antispasmodic-sedative therapy

Ingredient	Barbidonna Elixir & Tablets	Barbidonna No. 2 Tablets	Barbidonna D.A. Tablets
	per fl. dm. or tablet	Per Tablet	Per Tablet
Phenobarbital	¼ gr. (16 mg.)	½ gr. (32 mg.)	¼ gr. (16 mg.)
Hyoscyamine Sulfate	0.1286 mg.	0.1286 mg.	0.1286 mg.
Atropine Sulfate	0.0250 mg.	0.0250 mg.	0.0250 mg.
Hyoscine Hydrobromide	0.0074 mg.	0.0074 mg.	0.0074 mg.

Barbidonna D.A. tablets in a.c. dosage release the alkaloids immediately before the meal and phenobarbital after the meal.

VANPELT & BROWN, INC. RICHMOND, VIRGINIA

NOW... the first truly effective and safe control of both **chronic** and acute **diarrhea**

Sorboquel T.M.

(polycarbophil-thihexinol methylbromide)

IN CONVENIENT TABLET FORM

A totally new agent, for non-opiate control of the dual problem of diarrhea: too fluid feces, too frequent evacuations

Unexcelled therapeutic response, 85% of the chronic cases, 93% of the acute.[1-8]

The culmination of a decade of laboratory experimentation and over five years of clinical confirmation.

For too fluid feces, an extraordinary ability to absorb free fecal water.

For too frequent evacuations, superior, yet selective, antimotility action.

Convenient tablet form; simple, uncomplicated dosage schedule (1 tablet q.i.d.).

Even where all other agents have failed– Sorboquel arrests long-standing, uncontrolled, exhausting diarrheas

Unexcelled Therapeutic Response: Results of the Administration of Sorboquel Tablets[1-6]

	No. of Patients	*Response*		
		Excellent	*Good*	*Poor*
Chronic Diarrhea*	**485**	335	76	74
		84.7%		15.3%
Acute Diarrhea**	**332**	288	22	22
		93.4%		6.6%

*Chronic diarrheas include irritable bowel syndrome, regional enteritis, diverticulitis and ulcerative colitis, postantibiotic enteritis, malabsorption syndrome, radiation proctitis, surgically short-circuited intestinal states. Diarrhea had persisted for more than a year in a large percentage with bowel movement frequency averaging from 5 to more than 10 a day. In most patients, SORBOQUEL controlled the condition within 3 days, even where other agents had failed.

**Acute diarrheas include nonspecific gastroenteritis, enteritis, enterocolitis. Control of the diarrhea was achieved within 24 hours in most cases.

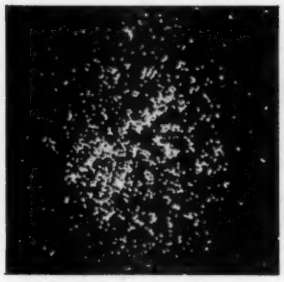
Dual-action **Sorboquel** arrests diarrhea even where all other agents have failed

The components in Sorboquel: the culmination of many years of development

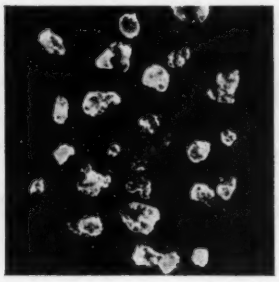
SORBOQUEL Tablets combine two unique and hitherto unavailable antidiarrheal agents—polycarbophil and thihexinol methylbromide. Acting together, through different but complementary mechanisms, these components in SORBOQUEL *absorb* free fecal water and *quell* hypermotility and associated spasm to an exceptional degree.

For too fluid feces, an extraordinary ability to absorb free fecal water

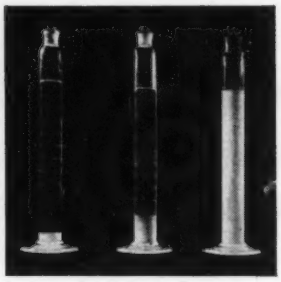
(through the hydrosorptive action of new polycarbophil)



Dry State
Demonstration of the particulate nature of dry polycarbophil.



Swollen State
Note the particulate nature of swollen polycarbophil. Impaction is virtually impossible.



(a) (b) (c)

Demonstration of the dependence of swelling of polycarbophil on pH (a) pH of stomach; (b) pH of duodenum; (c) pH of intestines.

A newly synthesized macromolecular substance exhibiting extraordinary capacity for absorption and retention of free fecal water[9-11] ▪ the colloidal suspension is free-flowing, since, in the swollen or hydrated state, the particulate structure is retained[9] ▪ exerts marked hydrosorptive action only on reaching the alkaline medium of the small intestine and colon ▪ virtually free of impaction qualities ▪ pharmacologically inert, not absorbed from the gut[12]

Convenient tablet form; simple, uncomplicated dosage schedule

SORBOQUEL DOSAGE: For older children and adults, initial dosage of one SORBOQUEL Tablet q.i.d. is usually adequate. Severe diarrheas may require six, or even eight, tablets in divided daily doses. (Dosages exceeding six tablets a day should not be employed over prolonged periods.) Many patients can be maintained on one to three tablets daily after the diarrhea is brought under control.

SIDE EFFECTS: The incidence of side effects at recommended dosage is negligible. (The usual precautions when using parasympatholytic agents should be observed. *Complete information regarding the use of* SORBOQUEL TABLETS *is available on request.*

DUAL ACTION

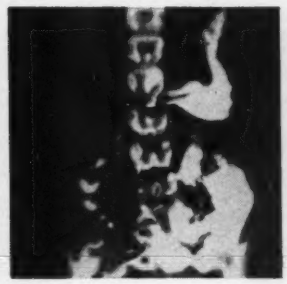
Sorboquel

TABLETS

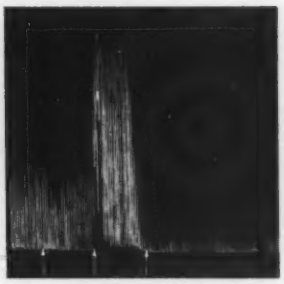
the first truly effective agent to control the dual problem of diarrhea: too fluid feces, too frequent evacuations

For too frequent evacuations, superior, yet selective, antimotility action
(through the parasympatholytic action of thihexinol methylbromide)

90-minute film demonstrating hypermotility of gastrointestinal tract in patient.



6-hour film after administration of thihexinol to patient showing marked inhibition of gastrointestinal motility.



(a) (b) (c)

Inhibition of methacholine-induced spasm by thihexinol in isolated rabbit intestine. Time of graph is 40 minutes. (a) normal motility; (b) methacholine, 40 mcg./L; (c) thihexinol, 10 mcg./ml.

A new, superior parasympatholytic agent with a dominant inhibitory action on intestinal motor function[12-16] ■ onset of intestinal motor inhibition has been shown to occur within *10-20 minutes*[14] ■ does not interfere with gastric secretion or digestive processes ■ unusually free from atropine-like side effects ■ its enteral antimotility action permits polycarbophil to exert maximal water-binding effect

SUPPLIED: SORBOQUEL TABLETS, bottles of 50 and 250. Each tablet contains 0.5 Gm. polycarbophil and 15 mg. thihexinol methylbromide.

REFERENCES: 1. Hock, C. W.: Med. Times 88:320 (March) 1960. 2. Winkelstein, A.: Personal communication. 3. Berkowitz, D.: in press. 4. Lind, H. E.: Personal communication. 5. Seneca, H.: in press. 6. Riese, J. A.: Personal communication. 7. Gilbert, A. S.; Schwartz, I. R., and Matzner, M. J.: Submitted for publication. 8. Personal communications to Medical Department, White Laboratories, Inc. 9. Pimparker, B. D.; Paustian, F. F.; Roth, J. L. A., and Bockus, H. L.: To be published. 10. Texter, E. C.: Personal communication. 11. Clinical reports to Medical Department, White Laboratories, Inc. 12. Grossman, A. J.; Batterman, R. C., and Leifer, P.: J. Am. Geriat. Soc. 5:187 (Feb.) 1957. 13. McHardy, G.; Browne, D.; McHardy, R.; Bodet, C., and Ward, S.: Am. J. Gastroenterol. 24:601 (Dec.) 1955. 14. Shay, H.: Personal communication. 15. Hirsh, H.: Personal communication. 16. Bercovitz, L. T.: J. Am. Geriat. Soc. 5:940 (Nov.) 1957.

WHITE LABORATORIES, INC., *Kenilworth, New Jersey*

Lutrexin®

(H. W. & D. brand of lututrin) TABLETS

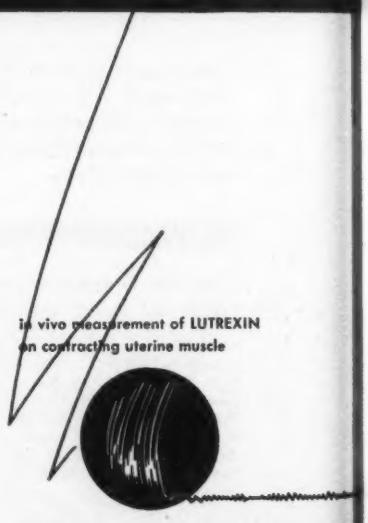
LUTREXIN has been used successfully in dysmenorrhea[1,2] for the past six years, as well as in premature labor[3,4] and threatened and habitual abortion[5,6].

LUTREXIN exerts an indirect, as well as a direct, relaxing action on the uterus by blocking the pituitary hormones.[7]

LUTREXIN administered orally decreases uterine contractions within thirty minutes.

LUTREXIN is a naturally occurring, non-steroid, uterine relaxing hormone, biochemically different from other ovarian hormones.

1. *Jones, G. S. and Smith, F.: Am. J. Obstet. Gynecol., Vol. 67, No. 3, 628-633, 1954.*
2. *Jones, Scott S.: Northwest Medicine, Vol. 54, 1253-1254, 1955.*
3. *Majewski, J. T. and Jennings, T.: Obstetrics & Gynecology, Vol. 5, No. 5, 1955.*
4. *Majewski, J. T. and Jennings, T.: Obstetrics & Gynecology, Vol. 9, No. 3, 1957.*
5. *Hardy, E. D.: to be published.*
6. *Trytball, S. W.: The Journal-Mich. State Med. Soc., p. 711, 1958.*
7. *Bryant, H. H.: to be published.*



In vivo measurement of LUTREXIN on contracting uterine muscle

HYNSON, WESTCOT & DUNNING, INC.

BALTIMORE 1, MARYLAND

Southern Medical Journal

PUBLISHED BY SOUTHERN MEDICAL ASSOCIATION

July 1960

The Clinical Usefulness of the Dye Dilution Curve*

ROBERT H. FRANCH, M.D.,† *Atlanta, Ga.*

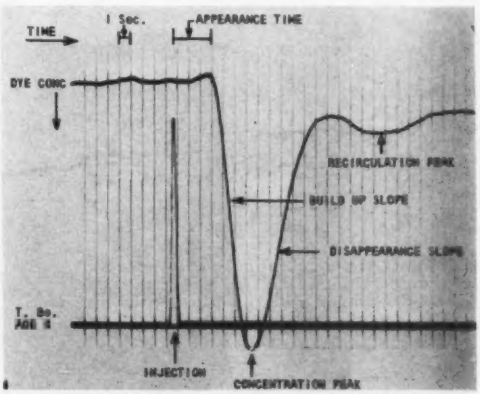
The use of the technics of dye dilution curves in conjunction with cardiac catheterization further extends the diagnostic accuracy of catheterization. The flow of dye within the heart, and the dilution curves obtained by studies of peripheral arteries offer a means of studying shunts.

DYE PARTICLES, injected into the circulation as a bolus and measured in the initial passage at a downstream site, distribute themselves in a time-concentration plot of grossly predictable form called a *dye dilution curve*. This presentation will concern itself with the detection and localization of central shunts by inspection of the directly recorded dilution curve. The methods of quantification of shunt flows using data from the dilution curve will not be considered. In practice, injection is made at a central site and measurement of concentration is made by a channel densitometer from a peripheral artery or by an ear oximeter. The output from the sampling photocell is led to a suitable recorder and the curve is described for immediate inspection to determine the presence or absence of abnormal circulatory pathways.

Detection of Central Shunts

Figure 1 shows a normal dilution curve. Five milligrams of Evan's blue dye was injected by catheter into the pulmonary artery of an 8 year old girl with valvular pulmonic stenosis; the dye concentration is continuously monitored by a photoelectric cell attached to the pinna of the ear. Each vertical line represents one second. Note the uninterrupted build-up slope, the sharp concentration peak, the steep disappearance slope (short disappearance time) and the prominent recirculation peak.

FIG. 1



A normal dye dilution curve in an 8 year old girl with valvular pulmonic stenosis.

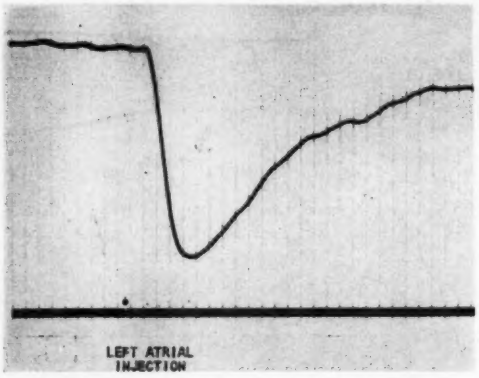
The two major types of distortion produced by *central shunting* are illustrated in a 7 year old girl with atrial septal defect, ventricular septal defect and pulmonary hypertension. She had both left to right (2.8 L. per minute) and right to left (0.7 L. per minute) shunts. Figure 2 illustrates the typical curve produced by the arteriovenous, or left to right shunt. Note the decreased peak concentration of dye,

*Read before the Section on Medicine, Southern Medical Association, Fifty-Third Annual Meeting, Atlanta, Ga., November 16-19, 1959.

†From the Emory University Hospital Cardiac Catheterization Laboratory, Department of Medicine, Emory University School of Medicine, Atlanta, Ga.

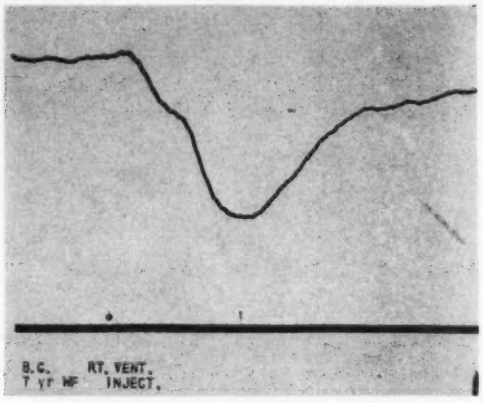
This study was aided in part by a grant from the Georgia Heart Association.

FIG. 2



Dye dilution curve characteristic of a left to right shunt.

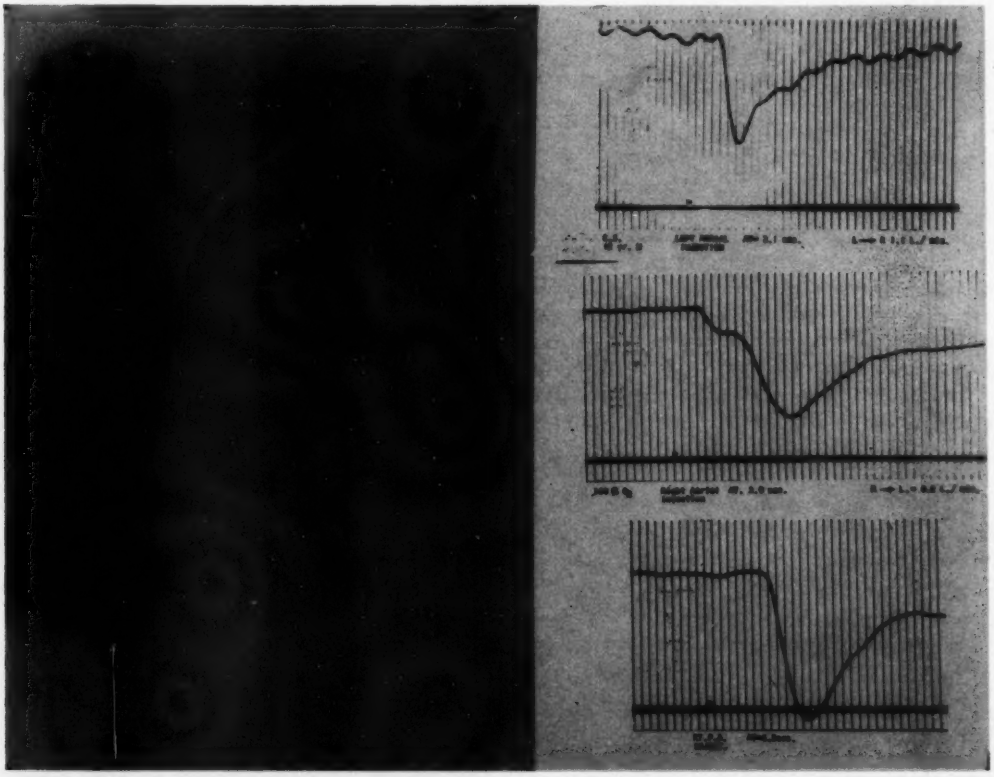
FIG. 3



Dye dilution curve characteristic of a right to left shunt.

the gentle disappearance slope (prolonged disappearance time) and the absence of the recirculation peak. These alterations are produced by recirculation of dye particles through the lungs resulting in a slow release of dye to the peripheral circulation. Figure 3 illustrates the typical curve produced by the veno-

FIG. 4



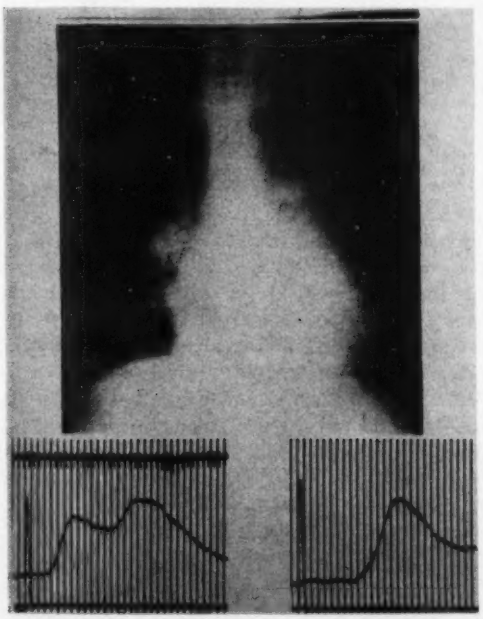
In the spot film, the tip of the catheter has passed from the right to the left atrium via an atrial septal defect. There is a prominent poststenotic dilatation of the pulmonary artery. (See text.)

arterial or right to left shunt. Note that the build-up slope is deformed by an abnormal, early appearing hump or deflection representing dye that has been shunted from the right ventricle via a ventricular septal defect into the left ventricle and aorta.

Localization of Central Shunts

Localization of the shunt site requires comparison of injections made proximal or at the site of the shunt with those made distal to the site of shunt. In a 12 year old boy with pulmonic stenosis and atrial septal defect with bidirectional shunt (Fig. 4), a peripheral dye curve following right atrial injection showed early deformity of the build-up slope not seen in curves recorded following right ventricular and pulmonary artery injections. The small right to left shunt is thus established to be at the atrial level. Localization of a left to right shunt is more difficult since an injection site on the left side of the heart is required to inject dye distal to the site of left to right flow. The catheter tip has passed via the atrial septal defect allowing access to the left atrium and left ventricle. Note that the left atrial injection demonstrates a left to right shunt; however, a curve recorded from the left ventricle was normal. The left to right shunt is thus established to be at the atrial level. The irregularities in the left atrial curve are related to changes in the magnitude of right to left shunt with respiration. Changes in the concentration of reduced hemoglobin cannot be distinguished from changes in the concentration of blue dye by the densitometer. Administering 100% oxygen minimizes this respiratory variation in peripheral arterial oxygen saturation. A new tricarbocyanine green dye uninfluenced by changes in the concentration of reduced hemoglobin avoids this problem.

FIG. 5



PA teleoroentgenogram of the heart shows an enlarged main and right descending pulmonary artery. The injection of dye was made into the right atrium (curve to the left) and into the right ventricle (curve to the right).

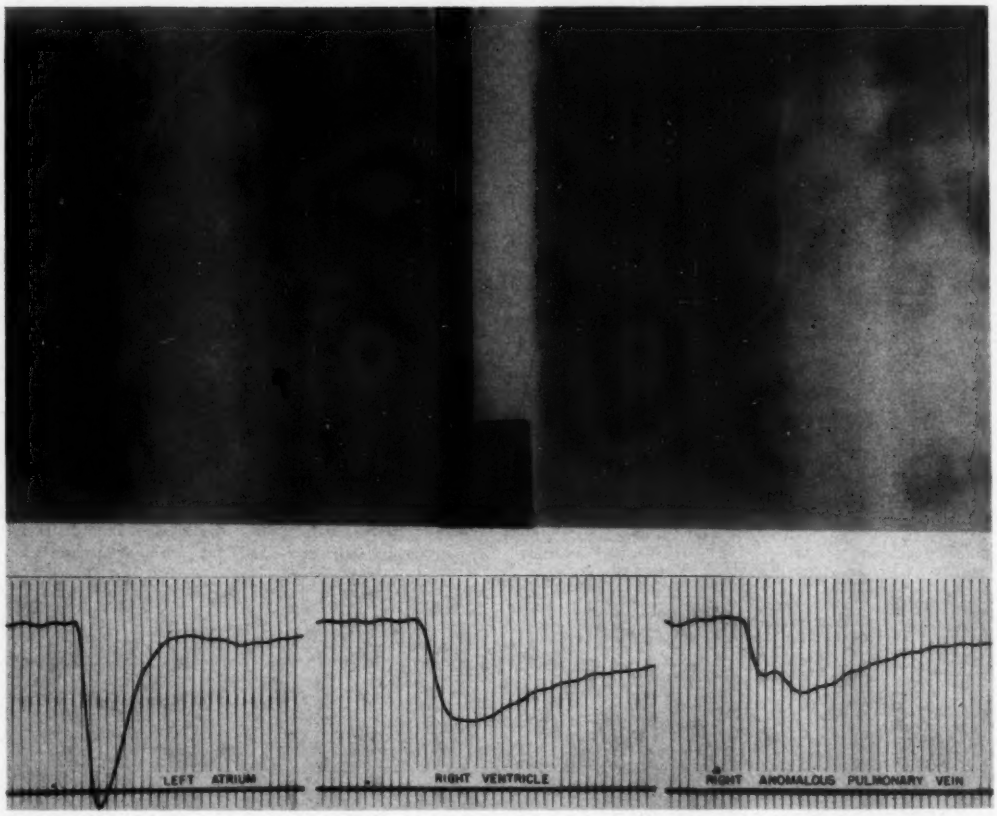
In a 44 year old truck driver, with clubbing and severe pulmonary hypertension, catheter exploration and sampling of central blood did not localize the site of shunt (Fig. 5). A peripheral curve following right atrial injection showed much dye appearing early, and an abnormal hump of the build-up slope into two peaks; right ventricular injection showed a normal build-up slope.* Atrial localization for the right to left shunt was thus established.

The accurate localization of shunts may occasionally be subject to error related to streaming of dye forward or backward from the chamber of injection. If the catheter tip in the left atrium is at the mitral valve, then the entire dye bolus may be injected into the left ventricle as in a 33 year old woman with atrial septal defect and anomalous pulmonary veins, who shows a nearly normal peripheral dye dilution curve following a left atrial injection (Fig. 6). It might be mistakenly assumed then, that a patent foramen ovale permitted ingress to the left atrium. At operation, a high atrial septal defect was associated with right anomalous pulmonary venous drainage (sinus venosus defect). Note the shunting of a portion of the blood draining from the right anomalous pulmonary vein across the atrial septal defect and its early appearance peripherally.

If the tip of the catheter is in the left ventricle immediately beneath the mitral valve, a portion of the bolus of dye may appear retrograde in the left atrium. A 12 year old girl with a simple atrial septal defect at operation showed a large decrease in peak concentration

*Depending on individual preference and/or detecting setup, dye curves may be recorded either with the concentration peak pointing to the top or to the bottom of the paper.

FIG. 6



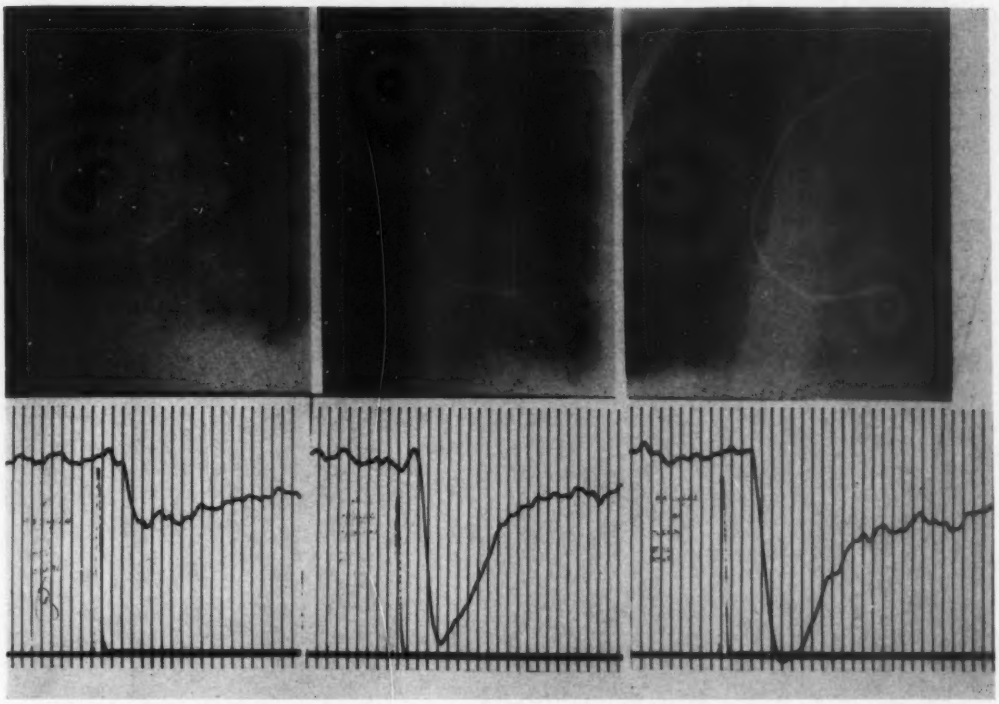
The arrow on the spot film on the left indicates the position to which the catheter tip was withdrawn for the left atrial dye injection. In the second spot film, the catheter tip is in a right anomalous pulmonary vein entering the upper right atrium near the superior vena cava. The dilution curve recorded from injection into the anomalous vein resembles one from the superior vena cava injection, but has a shorter appearance time than does the curve following right ventricular injection.

and a flat disappearance slope following an injection in the mid-left atrium (Fig. 7). When the tip of the catheter is just above the mitral valve, note that the peak concentration increases and the disappearance slope steepens suggesting partial streaming into the left ventricle. With the tip in the left ventricle near the mitral valve, peak concentration increases slightly, but the curve is similar to that from a left atrial injection near the mitral valve, falsely suggesting an additional shunt or a defect in the mitral leaflets.

Identification of Vessels and Flow Pathways

The catheter tip may enter the root of a great vessel whose identity cannot be determined by the catheter's position or by determinations of pressure or oxygen content. In a 6 year old boy (Fig. 8) with ventricular septal defect and right ventricular hypertension, a large root vessel occupying the usual position of the pulmonary artery was entered with the catheter tip from the right ventricle. The tip then passed into the descending aorta as if via an aortopulmonary communication. The catheter was withdrawn and dye was injected in the root of the great vessel in question. The early appearance time compared with the appearance time of injected dye from the right ventricle indicated the vessel to be aorta. The unidentified root vessel was thus found to be the anterolateral aorta of corrected transposition of the great vessels. Despite the irregular baseline secondary to respiratory fluctuations in oxygen saturation, the steep disappearance slope suggests no significant aortic left to right

FIG. 7



Each spot film demonstrates the injection site for the curve beneath it. On the left, the catheter tip is in the upper left atrium, the middle film shows the tip in the lower left atrium near the mitral valve; in the last film, the tip has passed across the mitral valve into the left ventricle.

shunt, thus excluding an aortopulmonary communication.

If the catheter tip enters a pulmonary vein well within the heart borders, question arises as to whether the drainage is proper. The peripheral dye dilution curve resolves this problem since an injection made into an improperly draining pulmonary vein resembles one made into the venae cavae.

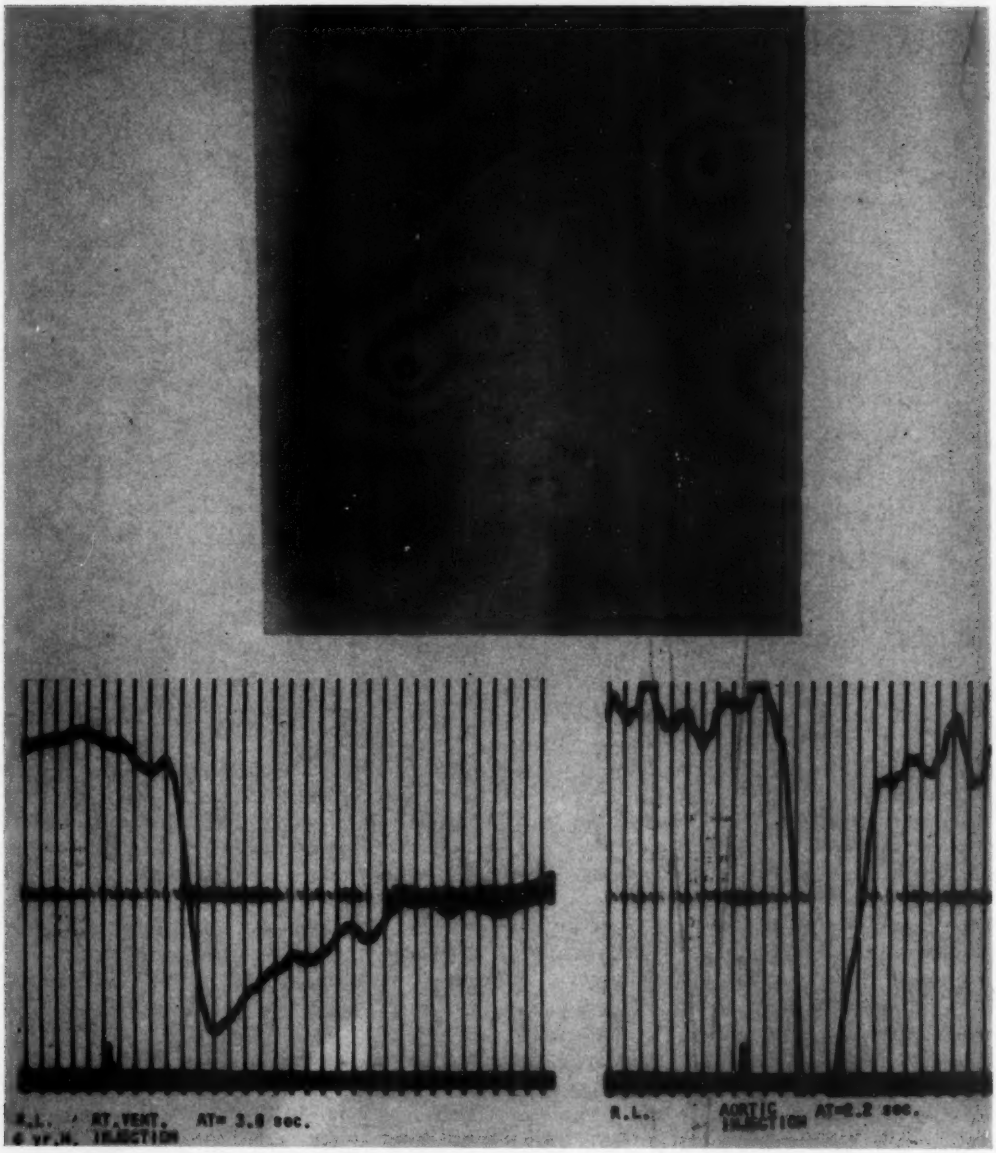
In pulmonary atresia, the heart ejects via a single great vessel, the aorta. The contour of dilution curves following injection from the right ventricle and the aorta are similar, and may be used to define a single outlet heart as in a 4 year old boy with pulmonary atresia (Fig. 9). The left to right shunt is related to a small patent ductus arteriosis and/or to bronchial collateral flow. In tetralogy of Fallot, right ventricular and aortic curves are dissimilar. Note the tall early appearing peak representing dye shunted into the aorta from the right ventricular injection site followed by a second smaller peak representing dye that has passed through the lungs (Fig. 10).

In tricuspid atresia, the blood flow to both ventricles comes by a common path across the mitral valve. The contour of dilution curves following injection into the right atrium and left atrium of a 12 year old boy are similar (Fig. 11), and may be used to determine whether tricuspid atresia is present, especially if the tricuspid valve cannot be crossed with the catheter tip.

Other Uses

Unusual venospasm in one adult and previous surgical ligation of the superior vena cava with persistence of the left superior vena cava in another, prevented complete right heart catheterization from the upper extremities. A normal dye dilution curve excluded significant shunting making catheterization, via a saphenous cutdown, unnecessary. At the operating table, the presence of an obscure ventricular septal defect associated with pulmonic stenosis and balanced shunt can be detected by an abnormal dye curve following the relief of the stenosis. Too, the adequacy of repair of

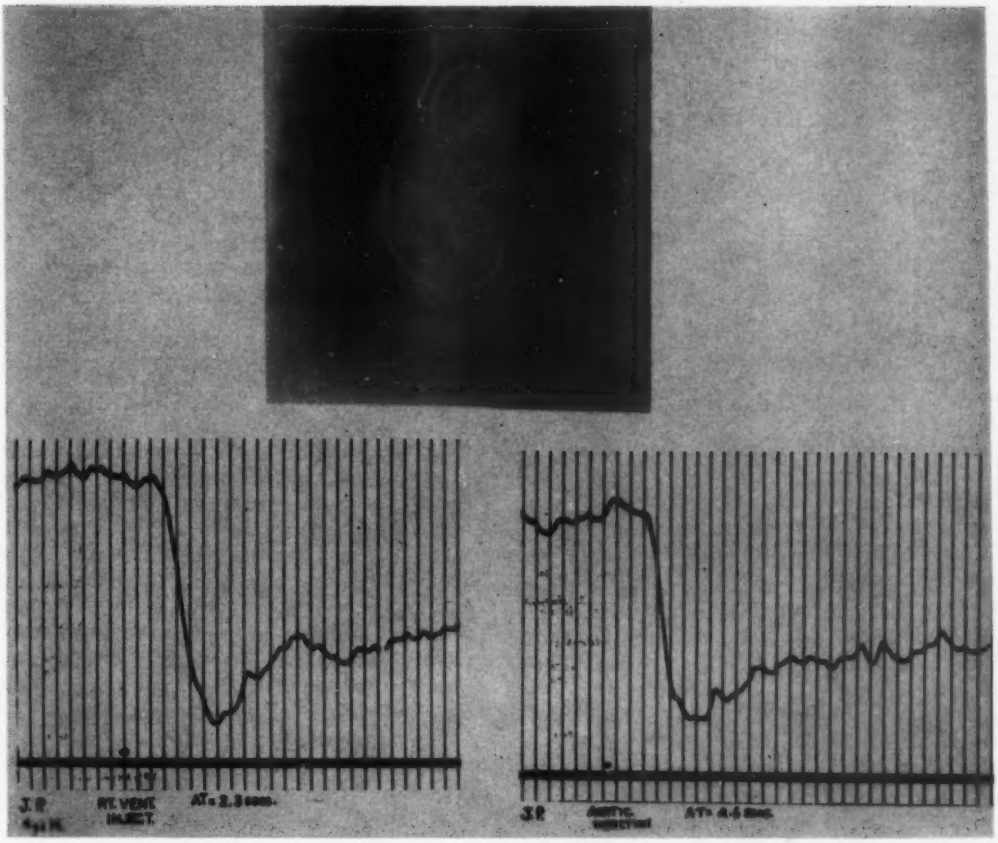
FIG. 8



In the spot film the catheter tip has passed from the right ventricle to the aorta via a ventricular septal defect in a case of corrected transposition of the great vessels.

a shunt defect may be determined while the chest is open. The long-term evaluation of the complete repair of septal defects can be simplified by comparing preoperative and postoperative dye curves. A large peripheral arteriovenous fistula may be associated with an abnormal dye dilution curve; however, a pulmonary arteriovenous fistula will have a normal dye dilution curve. Injected dye is washed to and fro across an incompetent valve, resulting in slow clearance of the dye from the heart; hence, a dilution curve in severe valvular insufficiency tends to resemble that of a left to right shunt.

FIG. 9

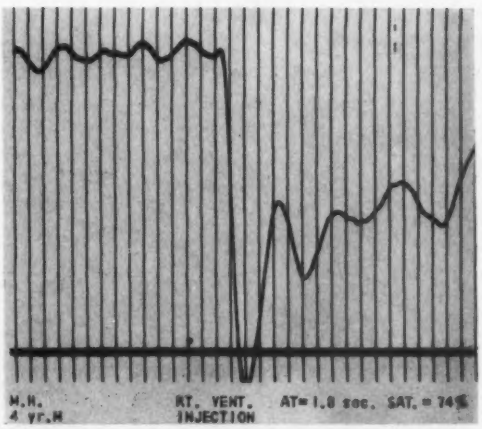


The catheter tip has passed from the right ventricle to the aorta via a ventricular septal defect.

Discussion

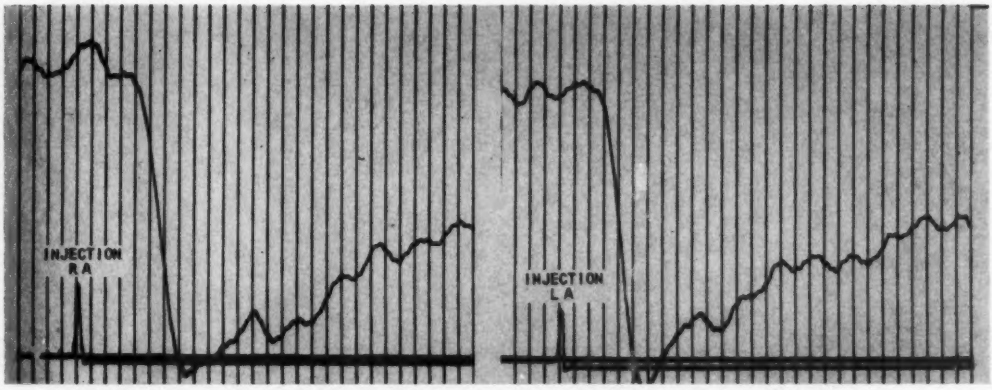
Simultaneous peripheral arterial dilution curves following central injection in a 12 year old boy with aortic stenosis (Fig. 12), do not appear abnormal, yet both dilution curves and multiple sampling at right heart catheterization have overlooked a left to right shunt, 15% of pulmonary flow. The search for increased sensitivity in detection of small left to right shunts has led to much ingenious methodology. The use of tricarbocyanine green dye with peak absorption at an isobestic point for both reduced and oxyhemoglobin and, thus, relative insensitivity to fluctuations in oxygen saturation has made right heart (venous) dye dilution curves possible.[1] Following an injection into a distal lobar pulmonary artery catheter, a shunt as small as 5% of pulmonary flow may be detected by a second proximal catheter

FIG. 10



Dilution curve from a right ventricular injection in tetralogy of Fallot shows a prominent early appearance peak.

FIG. 11



Note the similarity in dilution curves from right atrial and left atrial injections in tricuspid atresia.

sampling from the main pulmonary artery. In a left to right shunt, the venous return curve from the main pulmonary artery sampling site shows an early appearance peak. For localization, the sampling site is moved retrograde until early dye is no longer detected.[2]

Only a single catheter is required if a radioactive gas, methyl iodide (I^{131}), is introduced into the left heart by a single inhalation. In a left to right shunt, appearance at the pulmonary artery catheter and in sites distal to the shunt significantly precedes the appearance of gas proximal to the left to right shunt.[3] Similarly, a single breath of 100% nitrous oxide may be detected by gas chromatography from right heart blood samplings.[4] Too, hydrogen gas may be inhaled with direct detection by a catheter tip electrode.[5] Simultaneous sampling from the pulmonary artery and a peripheral artery during a 30 second inhalation of the inert radioactive gas, krypton (Kr^{85}), may also be used to detect small left to right shunts. In normals, the venous to arterial ratio of radioactivity is less than 15%, and in abnormal situations, nearly always greater than 20 per cent.[6] Recording isotope dilution curves directly by precordial counting is not adequate for detecting small left to right shunts. The ear oximeter avoids arterial blood letting, but may give a damped response to injected dye, making interpretation of the curve difficult (Fig. 13).

Peripheral dye dilution curves following

FIG. 12

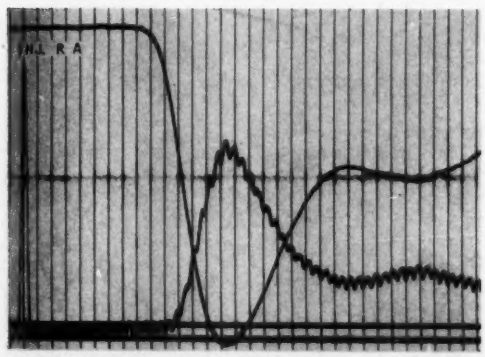


Figure shows the simultaneous recording of apparently normal dye dilution curves from the radial and femoral arteries of a 12 year old boy. The asymmetry of concentration peaks is related to differences in densitometer sensitivity.

FIG. 13

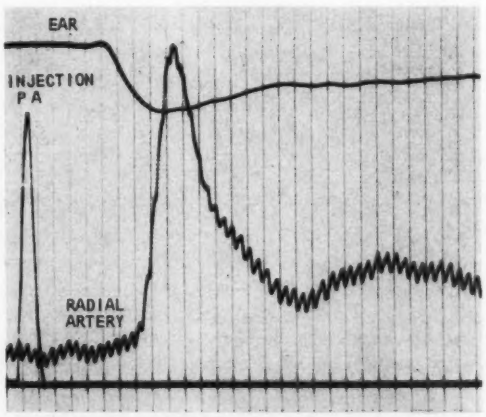


Figure illustrates simultaneous dye dilution curves from the ear and radial artery in a patient with a small left to right shunt. Note the prolonged build-up slope and the damped appearance of the ear oximeter tracing. The radial artery appearance time is uncorrected for tubing distance to the photocell.

central injection are highly successful in detecting small right to left shunts (5% of the systemic flow). The detection of the early appearance of fluorescein at the histamine prepared ear under Wood's light following an injection of 2 cc. of the 20% solution, or the decrease in arm-facial paresthesia time following ether injection were among the first circulatory measurements in veno-arterial shunts. Since then numerous dyes have been used, concentrated saline detected by a conductivity cell in blood, ascorbic acid detected by the Clark electrode, and in addition P^{32} labeled red blood cells and radioactive Renografin have been used as indicators. Radioactive krypton (Kr^{85}) in solution injected centrally is detected in high concentration in arterial blood in a right to left shunt. Normally, 95% of the gas is cleared in one passage through the lungs and the arterial concentration is low. Kr^{85} may be detected early in expired air following a left heart injection proximal to the site of left to right shunt.[7]

Summary

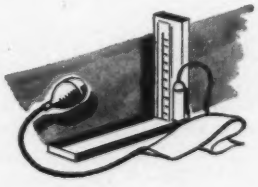
The direct recording of dye dilution curves using multiple injection sites in 300 cases studied at right heart catheterization has been useful in demonstrating the presence, direction and site of significant central shunts, in locating the catheter tip, whether in chambers or great vessels of the pulmonary or systemic circuit, or in anomalous channels, and in defining pathways of blood flow within the heart and its trunk vessels.

References

1. Wood, E. H., Swan, H. J. C., Fox, I. J., Kirklin, J. W., Helmholtz, H. F., Jr., Brooker, L. G. S., Heseltine, D. W., Essex, H. F., Burchell, H. B., Wright, L. J., Penido, J. R. F., Weil, M. H., Birkhead, N. C., Toscano-Barboza, E., and Woodward, E., Jr.: Symposium on Diagnostic Applications of Indicator-Dilution Technics, Proc. Staff Meet. Mayo Clin. 32:463, 1957.
2. Wood, E. H., Swan, H. J. C., Burchell, H. B., Linder, E., Birkhead, N. C., Guidry, L. D., Ledbetter, L. K., Daugherty, G. W., Semler, H. J., Brandenburg, R. O., and Weidman, W. H.: Symposium on Diagnostic Applications of Indicator-Dilution Curves Recorded from the Right and Left Sides of the Heart, Proc. Staff Meet. Mayo Clin. 33:581, 1958.
3. Amplatz, K., Marvin, J., Winchell, P., Gomez, G., and Adams, P.: Simple Isotope Dilution Technic for Evaluation of Congenital Heart Disease, Proc. 32nd Scientific Sessions Am. Heart Assoc. p. 663, Oct. 1959.
4. Ramsey, L. H., and Sell, G. C.: Use of Gas Chromatography in Detection and Location of Left to Right Shunts in Man, Proc. 32nd Scientific Sessions Am. Heart Assoc. p. 754, Oct. 1959.
5. Clark, L. C., Jr., and Bargeron, L. M., Jr.: Detection and Direct Recording of Left to Right Shunts with the Hydrogen Electrode Catheter, Surgery 46:797, 1959.
6. Sanders, R. J., and Morrow, A. G.: The Identification and Quantification of Left to Right Circulatory Shunts, Am. J. Med. 26:508, 1959.
7. Long, R. T. L., Braunwald, E., and Morrow, A. G.: Detection and Localization of Cardiac Shunts with Injections of Kr^{85} Solution, Proc. 32nd Scientific Sessions Am. Heart Assoc. p. 730, Oct. 1959.

Discussion (Abstract)

Dr. B. Woodfin Cobbs, Atlanta, Ga. I would like to thank Dr. Franch for his excellent presentation. It was about 30 years ago, when Professor Hamilton, working at the University of Louisville, perfected his formulas for estimating blood flow by the single injection indicator dilution technic. Certainly no one at that time had any idea that the method would become so extremely useful in clinical medicine. Ten or more years ago, Dr. Earl Wood at the Mayo Clinic first realized that changes in the shape of the dye curves could be used to detect the intracardiac shunts that occur in congenital heart disease. He also showed that a shunt could be localized by making several injections at different points within the heart. We owe a tremendous debt to Dr. Wood and to his associates at the Mayo Clinic. Recent refinements developed by the Mayo group, such as the dye Fox Green and the double catheter sampling technic, have made it possible to detect and measure intracardiac shunts more accurately than by any other method. In fact, a set of dye dilution curves now can give us more information about a patient with congenital heart disease than any other single test. Attempts have been made to measure the amount of leak in valvular regurgitation. Unfortunately, so far there is no satisfactory way to do this. The excellent group at Bethesda have introduced the inhalation of radioactive gases to diagnose certain intracardiac shunts. But in spite of these recent elaborations, the basic principles of dye dilution work are the same as sketched out 60 years ago by Dr. Stewart in Cleveland. And all our modern formulas are adaptations of those derived by Hamilton. Certainly this is an instance of how pursuit of a fine point in basic physiology has paid great clinical dividends. But it also shows just how far behind the times we clinicians are.



Physiologic Bowing of the Legs

MARY SHERMAN, M.D.,† *New Orleans, La.*

Bowlegs as a physiologic phenomenon in early childhood is not uncommon. It may appear as a familial tendency and not unusually is accompanied by hypermobility of joints. Normally physiologic bowing is corrected spontaneously, at times with overcorrection in terms of knock-knee. In any event, treatment by the doctor is rarely indicated. His greatest problem is that of putting the parents' minds at rest by continued reassurance.

FAMILIAR IN ANY OFFICE PRACTICE is the child who, when he begins to walk, is noted to be bowlegged and pigeon-toed. If the child shows no evidence of constitutional disease, and if he does not demonstrate real dysplasia, the question arises as to whether this child is truly abnormal. The numerous explanations advanced for this condition, the equally numerous and often contradictory types of therapy that are fiercely championed, and the fact that we do not see great numbers of adults with significant bowing of the legs give pause to wonder.

In the last 25 years many articles have been devoted to this problem. Böhm[1,2] early presented the idea that bowing of the legs, together with "rotational variation from the adult form," represents one phase of the development of normal children. He believed that this stage is customarily followed by a period of straightening and overcorrection which results in knock-knees. The knock-knees, in turn, straighten out spontaneously so that by the age of 6 or 8 years the healthy child usually has straight legs. Böhm recognized that an occasional child fails to achieve complete symmetry of the lower extremities, a condition which he explained on the basis of developmental arrest or incomplete evolution.

Blount[3] accepted Böhm's concepts of normal evolution and carefully distinguished this process from the epiphyseal disturbance that is associated with his name.[4] Blount believes that even some instances of moderately severe tibia vara will correct themselves spontaneously or with "conservative treatment." In the occasional patient whose bowed legs do not correct spontaneously by the age of 2 or 3 years, he recommends bracing at night and considers surgical treatment only as a last resort.[5]

A few authors[6-8] have called attention to the fact that even rather extreme degrees of infantile bowing will resolve spontaneously. Other investigators,[9-13] although they are willing to concede that nature is in general beneficent, still believe that treatment for infantile bowlegs is mandatory. The usual contention of these workers is that without early, rigorous treatment many children will grow into deformed adults.

Clinical Considerations

It is the purpose of this paper to sustain the thesis that it is possible to predict at the first visit the future course of most of these patients, and that the majority of them need no treatment. The 30 children on whom this report is based were all seen during the past 5 years in one Clinic of the State Crippled Children's Service. The course of all was followed by one examiner. The roentgenograms were made by one of two technicians and, as nearly as possible, by the same technic each time.

Although most of these children do not have a diet which, by modern standards, would be considered adequate, and although many of them exhibit moderate anemia, none has ever shown signs of serious nutritional disease or of epiphyseal disorganization. No child was treated and the majority went barefoot except in extremely cold weather. Every child came for examination (usually at the insistence of a nurse or doctor) because of bowed legs, with or without pigeon-toes, and every child now has straight legs or some degree of knock-knee. Excluded from this series were 3 children with such extreme

†From the Department of Orthopedics, Ochsner Clinic, New Orleans, La.

laxity of the joints that they were unable to walk without support, 4 children with congenital disturbances of the upper tibial epiphysis (tibia vara or "Blount's disease"), and several children with asymmetrical epiphyseal growth which followed trauma or infection.

The following cases are typical of all the others in the group.

Case 1. A white boy was first examined at the age of 17 months because of pronounced bowing of the legs. He was the youngest of 8 children. Three of his siblings had had bowed legs which had never been as severe as the patient's. This child had always had a good diet including adequate vitamin D since the age of 3 months. Figure 1 shows the bowing evident at the first visit and the straightening and slight overcorrection of the legs which had occurred by the time the child was 5 years old.

Case 2. This white boy, referred by a physician, was seen at the age of 16 months. The bowing of his legs had been noted at birth but seemed to be much more pronounced when the baby began to walk at 9 months of age. An older sister, who too had walked at 9 months had had bowed legs which had straightened spontaneously. Figure 2 shows the pronounced bowing at 16 months, and the mild degree of knock-knees at 5 years of age.

Case 3. This negro girl did not begin to walk until she was 15 months old. At that time bowing of the legs, much more severe on the left side, was noted. When the child had not improved noticeably at the age of 18 months, the parents brought her to the Clinic. She was one of the few who had always had an adequate diet, including vitamin supplements. Figure 3 shows the mild degree of knock-knee which was present when the child had reached 4½ years.

Figure 4 shows the same child at the age of 18 months and 4½ years.

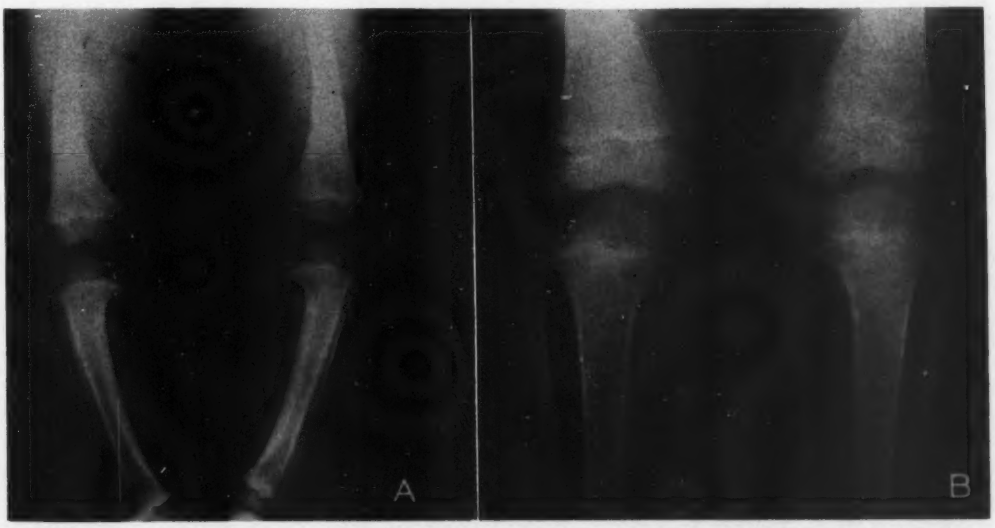
Case 4. This white girl was the youngest of 12 children. Three of her siblings had had severe bowing of the legs which had disappeared by the time they were 2 years old. For this reason the mother was not particularly concerned when this child, who began to walk at 10 months, did so with bowed legs and "rolling her feet over onto their sides." However, the combined protests of the neighbors and the district nurse brought the patient to the Clinic.

Figure 5 shows the bowing, which was striking enough when the child began to walk, the degree of spontaneous correction which had occurred 8 months later, and the straightening which was present when the child was 2 years old.

Comment and Discussion

Even Nachlas,[13] whose 1934 paper popularized the concept of medial tibial torsion as an atavistic developmental trait and the cause of bowlegs and pigeon-toes, commented that, "in adults it is seen only occasionally." In the sole article which attempts anything approaching a statistical analysis, it was shown that one third of 50 normal 2 year old children showed no external torsion and had

FIG. 1



(Case 1) (A) At 17 months, there is bowing of both femur and tibia, "beaking" of the upper medial tibia, thickening of the medial tibial cortex, and an upward and medial slant of the lower tibial epiphysis and ankle joint. Also there is overlapping of the shadows of tibia and fibula, which Nachlas considered as pathognomic of tibial torsion. (B) After 4 years all bowing has disappeared, there is only slight irregularity of the upper medial tibial metaphysis, the tibial cortex is normal and there is no overlapping of tibia and fibula.

FIG. 2

(Case 2) (A) At 16 months there are the same findings as shown in figure 1,A. (B) Four years later a mild degree of knock-knee is present, and all the previous "abnormalities" have disappeared.

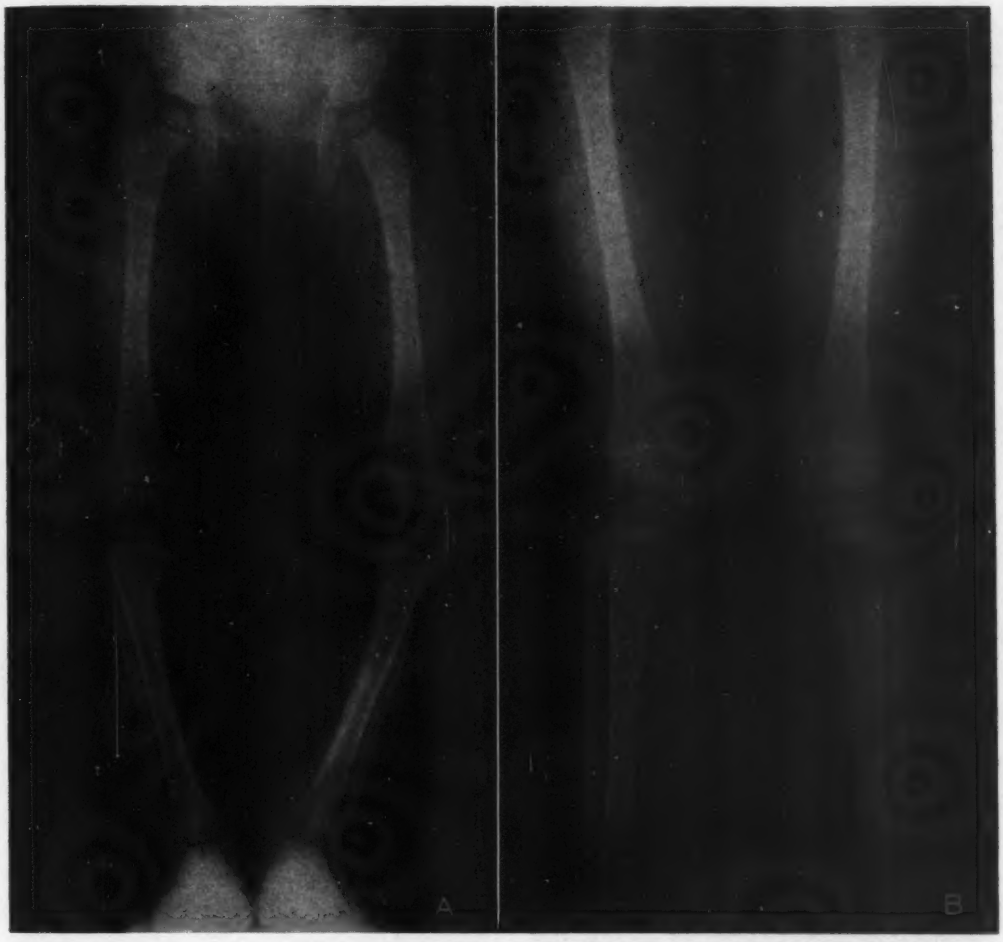
a pigeon-toed gait.[14] On the other hand, in a group of 200 normal adults, 8 had some degree of internal torsion but only 3 had significant functional interference that produced a pigeon-toed gait. All authors who recommend treatment agree that surgical correction for persistent "deformity" is seldom necessary. It would seem that the incidence of "deformity" resistant to treatment is about the same as that which is uncorrected by growth.

The children whom we have observed are, like those in other groups, generally healthy and often large and heavy. There is frequently a history of spontaneously corrected bowed legs and pigeon-toes in the parents and in siblings. Most of the patients exhibit some degree of bowing in both femur and tibia, but that of the tibia is always greater and is often accompanied by varying degrees of internal torsion.* The medial tibial cortex is thickened, "beaking" of the medial portion of the upper tibial epiphysis is usually prominent, and there is an upward medial plane of the lower tibial epiphysis and ankle joint. This is due to a relative increase in length of the fibula, and the pigeon-toed gait follows naturally. Pronation, if present, is usually at the ankle joint.

The most striking thing about many of these children (a point which has been men-

*It is of interest that when several examiners were asked to evaluate the degree of tibial torsion, the estimates not only varied by as much as 25° to 30°, but often there was no agreement as to whether torsion was internal or external.

FIG. 3



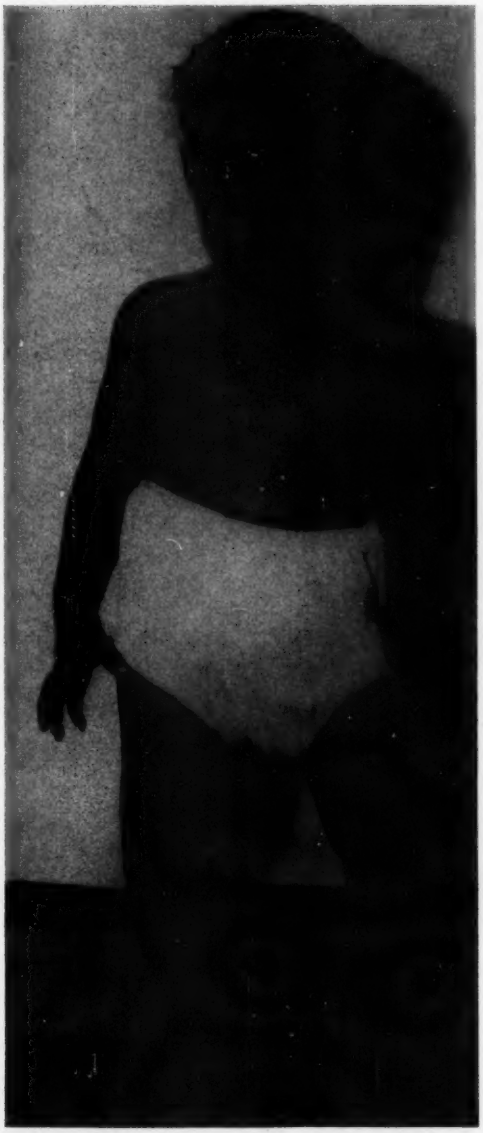
(Case 3) (A) At 18 months this child demonstrates the same findings. There is relatively less distortion of the femora in this case, and the bowing is greater on the left than on the right. (B) Two years later the bowing has been grossly overcorrected, and a knock-knee deformity is now present.

tioned only by Howorth[15]) is that all their joints are hyperflexible. This is just as obvious in the trunk and upper extremities as it is in the lower extremities. This fact probably accounts for the odd postures these children often assume. They are comfortable in positions which the average child cannot assume at all, let alone with comfort. It would seem logical to suppose that these postures are the result and not the cause of the child's physical constitution.

This same looseness of articular structures permits rotatory motion, particularly at the knee, a finding which has been well described by Rosen and Sandick.[16] In a careful study which employed anatomic and roentgenographic technics of measurement of tibial torsion, they concluded that in most children with pigeon-toed gait "the deformity is due to medial rotation of the entire leg at the knee." Our own observations are certainly in agreement with this statement.

If all the available facts are taken into consideration, a conservative estimate of the rate of spontaneous "cure" of physiologic bowlegs seems to be at least 95%, and it may well be higher. There is evidence that in a few families (without known disease) bowed legs,

FIG. 4, A



(Case 3) Corresponding photograph of the child whose roentgenogram is shown in figure 3,A.

with or without internal tibial torsion and pigeon-toes, are part of the genetic make-up.[17] It is difficult to see how any form of "conservative" therapy could alter the course of development of these individuals.

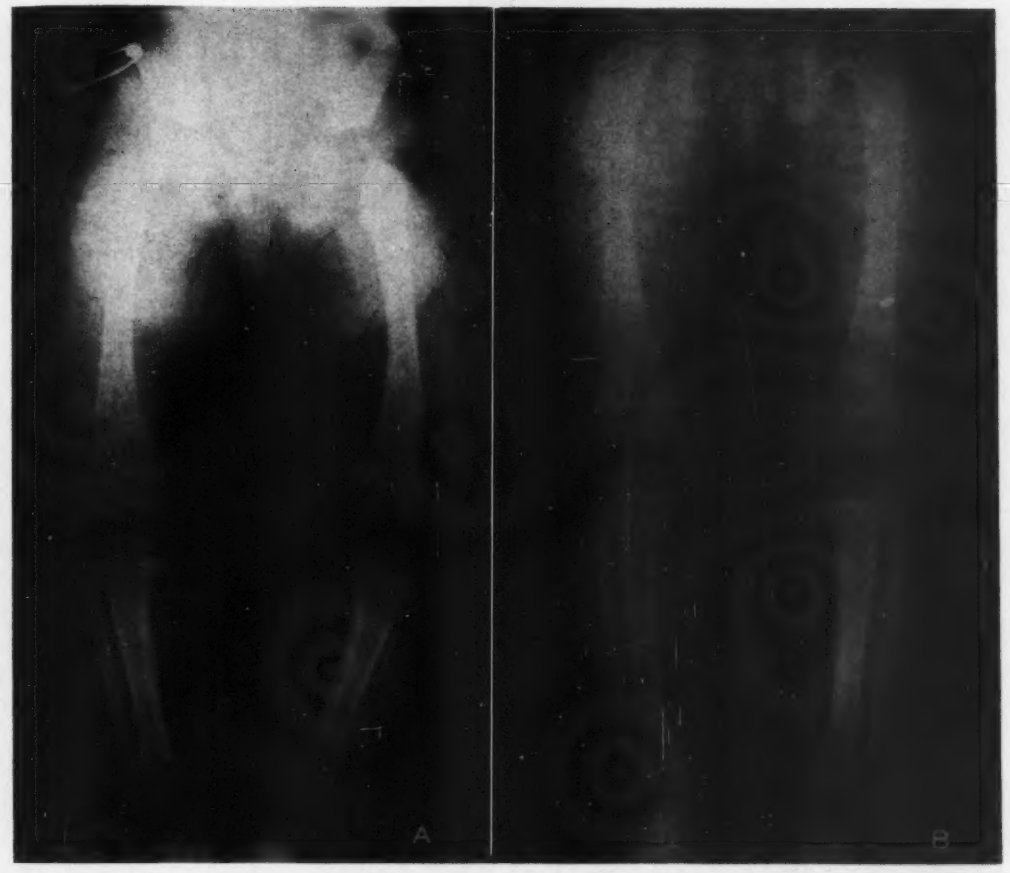
If these interpretations are correct, the entire question of treatment becomes superfluous, except for those few children who, instead of improving with age, become worse. There will be an occasional child, like the first one presented in Blount's original paper, who starts out looking like a child with ordinary physiologic bowing, and there will be another whose genes have already determined continued abnormal growth. It will fairly soon be evident that these few children will not resolve their difficulties spontaneously and treatment, which will probably need to be more than "conservative," can be directed to them.

Surely it is not reasonable to encumber all

FIG. 4, B

(Case 3) Corresponding photograph of the child whose roentgenogram is shown in figure 3,B.

FIG. 5



(Case 4) (A) In this roentgenogram, made at 15 months, the condition had already begun to improve; the same findings are demonstrated, however. Particularly striking are the thickening of the medial tibial cortex and the tilt of the lower tibial epiphysis and ankle joint. (B) Six months later the limbs appear straight, although the bony alterations have not yet disappeared completely.

the other babies who have bowed legs and pigeon-toes with orthopedic shoes and braces! It is true, as Burrows[18] said, that "advice to do nothing demands far more careful explanation than advice to do something, and due warning against the well-meant prompting of friends." Such a careful explanation will usually gain the cooperation of the parents, and later their gratitude to a physician who, again with Burrows,[18] supports the SLPLBA (Society for Leaving the Poor Little Blighters Alone).

Acknowledgment

All phases of this investigation were greatly aided by Mrs. May Jeanne Stewart of the Louisiana State Health Department.

References

1. Böhm, M.: Infantile Deformities of the Knee and Hip, J. Bone & Joint Surg. 15:574, 1933.
2. Böhm, M.: Das menschliche Bein, (Band 9 of Deutsche Orthopädie) Stuttgart, Ferdinand Enke, 1935.
3. Blount, W. P.: Bowleg, Wisconsin M. J. 40:484, 1941.
4. Blount, W. P.: Tibia Vara, Osteochondrosis, Deformans Tibiae, J. Bone & Joint Surg. 35:1, 1937.
5. Blount, W. P.: Personal communication.
6. Christie, A., and Stempfel, R. S.: Nonrachitic or Physiologic Bowing, Postgrad. Med. 17:306, 1955.
7. Forrest, H. J.: Physiologic Bowlegs, Arch. Pediat. 66:349, 1949.
8. Holt, J. F., Latourette, H. B., and Watson, E. H.: Physiological Bowing of the Legs in Young Children, J.A.M.A. 154:390, 1954.
9. Caldwell, G. A., Shorkey, R. L., and Duncan, T. L.: Treatment of Mild Knock Knees and Pronated Feet in Childhood. Results in 63 Cases, New Orleans M. & S. J. 104:304, 1952.
10. Kite, J. H.: Torsion of the Lower Extremities in Small Children, J. Bone & Joint Surg. 36-A:511, 1954.
11. Knight, R. A.: Developmental Deformities of the Lower Extremities, J. Bone & Joint Surg. 36-A:521, 1954.
12. Morris, H. D.: Treatment of Infantile Bowlegs and

Knock-knees, with Special Consideration of the Therapeutic Use of Large Doses of Activated Ergosterol. Analysis of 58 Cases, South. M. J. 44:435, 1951.
13. Nachlas, I. W.: Medial Torsion of the Leg, Arch. Surg. 28:909, 1934.
14. Hutter, C. G., Jr., and Scott, W.: Tibial Torsion, J. Bone & Joint Surg. 31-A:511, 1949.
15. Howorth, M. B.: Discussion of Knight, R. A.: Developmental Deformities of the Lower Extremities, J. Bone & Joint Surg. 36-A:521, 1954.
16. Rosen, H., and Sandick, H.: The Measurement of Tibiofibular Torsion, J. Bone & Joint Surg. 37-A:847, 1955.
17. Blumel, J., Eggers, G. W. N., and Evans, E. B.: Eight Cases of Hereditary Bilateral Medial Tibial Torsion in Four Generations, J. Bone & Joint Surg. 39-A:1198, 1957.
18. Burrows, H. Jackson: An Even Keel in Orthopaedics, Proc. Roy. Soc. Med. 46:805, 1953.

HOTEL RESERVATION APPLICATION FORM

FOR 54th ANNUAL SESSION

ST. LOUIS, OCTOBER 31-NOVEMBER 3, 1960

APPEARS IN THIS ISSUE

MAKE YOUR RESERVATIONS EARLY!

The Control of Intractable Pelvic Hemorrhage by Ligation of the Hypogastric Artery*

SAMUEL S. BINDER, M.D., and GEORGE A. MITCHELL, M.D.,†
Chattanooga, Tenn.

Under certain conditions of uncontrollable bleeding from the female genital tract, ligation of the hypogastric arteries may be justifiable. These circumstances have been considered by the authors, as well as the unlikelihood of ischemic necrosis from impaired blood supply.

IN SPITE OF ADVANCES made in the field of gynecology, hemorrhage continues to be one of the most vexing problems confronting the gynecologist. Whether this hemorrhage occurs at the time of operation, in the course of disease, or as a postoperative complication, it must be controlled in order to preserve life. No matter how many blood transfusions a patient may receive, or how much blood may be available, the prognosis obviously depends upon control of the source of the bleeding.

Everyone practicing gynecology will eventually be called upon to manage severe or intractable hemorrhage. Fortunately, the majority of these problems respond to direct measures of packing, ligation of bleeding points, and the use of hemostatic agents, with or without replacement of blood or blood fractions. Occasionally, the above measures are unsuccessful. We have encountered several such instances within three years and in each ligation of the hypogastric artery or arteries was mandatory for control of the bleeding.

The following case reports are illustrative:

Case 1. M. J. R., age 41, was admitted to the emergency room of Erlanger Hospital Jan. 9, 1957, in profound shock from vaginal blood loss.

Intravenous administration of 5% glucose containing norepinephrine (Levophed), and packing of the vagina with Oxycel gauze and plain gauze were used immediately while blood was being made available. A blood pressure of 122/90 was obtained one hour after the administration of 1,000 cc. of whole blood in addition to the above measures, but it was not sustained by additional transfusions, nor was the vaginal bleeding controlled. She was taken to the operating room where she was examined under light Pentothal-nitrous-oxide-oxygen anesthesia and found to have a major bleeding point at the top of the vaginal vault in a fungating, necrotic mass of tissue consistent with carcinoma of the cervix and invading the parametrium, with postirradiation fibrosis of the vagina below the site of the cervix. The bleeding point was electro-dessicated, and Oxycel and plain gauze packing was placed against the area.

Bleeding continued through the packing and, consequently, a laparotomy was performed. The pelvis presented dense adhesions, a hard mass where the uterus should be, absence of the adnexa, and absence of anatomic landmarks. Under the circumstances, any surgical procedure other than simple ligation of the hypogastric arteries was untenable.

An incision was made in the peritoneum overlying the right external iliac artery and carried cephalad to the bifurcation of the common iliac artery where the hypogastric artery was identifiable. The latter was dissected free of the internal iliac vein for 2 cm. below the bifurcation, and was doubly ligated with No. 1 chromic catgut sutures. The procedure was repeated on the left side, care being taken in both instances to avoid the ureters.

The vaginal bleeding ceased, and the packing was removed without recurrence. Her blood pressure remained at normal levels throughout recovery, and she was dismissed on the 9th hospital day in good condition.

It was learned later that the patient had been operated on in 1946 with removal of both oviducts and ovaries because of bilateral tubo-ovarian abscesses, and had been treated for Stage 2 carcinoma of the cervix by radium insertion and external radiation in the Tumor Clinic of Baroness Erlanger Hospital in March and April 1956.

Follow-up examinations revealed a rectovaginal fistula attributable to radiation necrosis, and not deprivation of blood supply by arterial ligation. By May 1957, the induration in the vaginal vault had

*Read before the Section on Gynecology, Southern Medical Association, Fifty-Third Annual Meeting, Atlanta, Ga., November 16-19, 1959.

†From the Departments of Obstetrics and Gynecology of the Erlanger and the Memorial Hospitals, Chattanooga, Tenn.

cleared and it presented no visible evidence of malignancy. The patient is still alive, but requires further treatment.

Case 2. P. M. L., a 42 year old gravida 9, para 8, was admitted Jan. 23, 1958, with the history of onset of labor 24 hours previously at approximately the 40th week of pregnancy (without prenatal care by the patient's election), and spontaneous rupture of the membranes 3 hours prior to admission, without vaginal bleeding.

Examination revealed a slightly dehydrated patient with a B. P. of 130/80, P. 96, and T. of 99°. The uterus apparently was of term-size with contractions of good quality at 8 minute intervals, of 35 seconds duration, and with fetal heart tones of good quality at a rate of 140 per minute. A sterile pelvic examination was performed on admission to the labor floor; the cervix was found to be long and thick, dilated approximately to 2 cm., and showed a purulent discharge at the external os. During the ensuing 3 hours, the contractions occurred at 5 minute intervals of 35 to 40 seconds duration, but of poor quality. A dilute solution of Pitocin in 5% glucose in distilled water was begun intravenously; the contractions improved in quality, occurring at 5 minute intervals of 45 seconds duration. At 5 hours after admission she had a chill with a rise in temperature to 102° F. and the Pitocin was discontinued. Blood pressure, pulse, and fetal heart tones remained within normal limits until 2 hours later, when a slight bloody show became apparent, accompanied by a decrease in B. P. to 80/60 and an increase in pulse rate to 120 per minute. Cervical dilation at this stage was 6 cm. and the fetal heart tones were changed in rate and became irregular. Oxygen and transfusions of whole blood were administered. The patient delivered spontaneously a stillborn fetus followed immediately by the placenta, suggesting an ablatio placenta. Vaginal examination revealed a laceration of the vaginal vault extending into the right broad-ligament with a large hematoma involving the area.

The patient was transferred to the operating room immediately and a laparotomy performed, with disclosure of a large retroperitoneal hematoma occupying the right broad ligament. A subtotal hysterectomy and salpingo-oophorectomy were done, revealing avulsion of the right uterine artery with retraction of the proximal end into the hematoma, prohibiting local ligation. Following the same procedure as in the previous case, the external iliac artery was followed to the bifurcation of the common iliac artery, and identification of the hypogastric artery made without difficulty even though it extended into the hematoma. Ligation with No. 2 chromic catgut was followed by cessation of bleeding, and ligation of the left hypogastric artery was unnecessary to maintain hemostasis. Blood pressure and pulse promptly returned to normal upon ligation of the artery and remained stable. The postoperative course was smooth, afebrile, and with slight icterus which cleared spontaneously by the 5th postoperative day. The patient was dismissed in good condition on the 9th postoperative day.

Total blood administered amounted to 3,500 cc.

Case 3. B. M., a 33 year old white gravida 4, para 3, abortus 0, woman in the 36th week of pregnancy was seen in consultation on Aug. 13, 1957, with the findings of abruptio placenta, apparently of 6 hours duration, without evidence of surgical shock, or history of external bleeding. There was an antepartum history of mild toxemia for the week preceding this episode, and a past history of congenital polycystic kidneys with repeated bouts of acute pyelitis.

The first external bleeding occurred shortly after admission, and consisted of a sudden gush of bloody amniotic fluid of 600 cc. Blood pressure and pulse remained within normal limits, but laboratory studies revealed a Hgb. of 7.5 Gm., a PCV. of 24%, and defective fibrinogen activity. Whole blood, fibrinogen, and dilute intravenous Pitocin (1 cc. of Pitocin in 1,000 cc. 5% glucose in water) were started on admission, and the membranes, which were still intact at the cervical os, were ruptured to permit escape of amniotic fluid to the outside rather than into the uterine sinuses.

The patient remained in good condition until 9 minutes after spontaneous delivery of a stillborn, premature male infant, when she promptly lapsed into surgical shock upon expulsion of 1,000 cc. of old blood, blood clots, and amniotic fluid. The uterus was atonic and remained refractory to oxytocics and intra-uterine packing. Accordingly, a total abdominal hysterectomy was performed as rapidly and with as little trauma as possible, with the removal of a classical Couvelaire uterus. Oozing from all cut surfaces was noted, but was insufficient to arouse concern over irreplaceable blood loss. Inspection at the end of the operation revealed brisk bright red vaginal bleeding, but this was satisfactorily controlled by placing sponge forceps on bleeding points in the vaginal cuff.

Subsequently, the patient stabilized at a B. P. of 110/60 and a P. of 92, but an hour after transfer to her room brisk vaginal bleeding was again noted. She was returned to the operating room where ligation of the branches of the left vaginal artery was successfully accomplished vaginally, but retraction of bleeding points on the right side into a large hematoma of the broad ligament made control of bleeding at that point impossible. Accordingly, the abdomen was reopened and the anterior division of the right hypogastric artery was identified and doubly ligated with No. 1 chromic catgut suture. Bleeding ceased abruptly and ligation of the contralateral hypogastric artery was unnecessary.

Her postoperative course was smooth, and with extensive supportive therapy, she was dismissed on the 17th postoperative day without evidence of ischemia of the tissues supplied by the right hypogastric artery.

Of interest, perhaps, is the fact that the patient received 10,000 cc. of whole blood and 12 Gm. of fibrinogen during the intrapartum and operative periods.

Discussion

Although the hypogastric artery is the chief blood supply to all major pelvic viscera, it apparently can be ligated without undue fear of ischemic necrosis.

In a review of this subject by Tajes[1] the studies of Wright and Shafiroff were quoted. The latter investigators, using radiopaque media, studied the collateral circulation of the hypogastric artery; the results of these studies showed the collateral circulation to be as follows:

1. The uterine artery branching from the hypogastric artery anastomoses with the ovarian artery.

2. The middle hemorrhoidal branch of the hypogastric artery anastomoses with the superior hemorrhoidal artery arising from the inferior mesenteric. The middle hemorrhoidal artery also anastomoses with the inferior hemorrhoidal, which is a branch of the internal pudendal artery, which, again, is a branch of the hypogastric artery.

3. The obturator artery, branching from the hypogastric artery, gives off pubic branches which anastomose with the inferior epigastric artery arising from the external iliac artery.

4. The inferior gluteals from the hypogastric artery anastomose with the circumflex and perforating branches of the deep femoral artery.

5. The superior gluteals from the hypogastric artery anastomose with the lumbar arteries from the aorta.

6. The iliolumbar arteries from the hypogastric anastomose with the lumbar arteries from the aorta.

7. The vesical arteries which supply the bladder are both branches of the hypogastric artery, and they anastomose with the uterine arteries, also from the hypogastric, and with the vaginal arteries.

The hypogastric artery has been ligated innumerable times in the course of radical pelvic surgery. There have been no arbitrary rules as to when the procedure should be done. Bastiaanse[2] stated that the hypogastric may be ligated in the course of radical hysterectomy whenever it is felt that the procedure will facilitate the operation. Much has been written in the foreign literature concerning this procedure, and there are a few interesting reports concerning palliative treatment of inoperable carcinoma of the cervix or uterus by ligation of the hypogastric arteries.[3-6] For example, Taylor and Peightal[7] describe a case of carcinoma of the cervix treated with cautery and ligation of the hypogastric arteries, with no evidence of growth four years after operation.

The majority of reports on ligation of the hypogastric artery deal with the treatment of hemorrhage from carcinoma of the cervix. The first English report was written by Kelly[8] in 1894.

Leventhal, Lash, and Grossman[9] reported the extraperitoneal technic of hypogastric ligation. This procedure was used by them in 5 cases of hemorrhage from carcinoma of the cervix. In all their cases bleeding either followed or occurred during the course of radiation therapy. Their article describes in detail the extraperitoneal approach to the hypogastric artery. Greenhill[10] also describes this technic in his book of *Surgical Gynecology*. This procedure requires two abdominal incisions to reach both arteries, the extraperitoneal approach probably being used to avoid peritoneal contamination.

Salzberg, Fuller, and Hoge,[11] in 1953, reported 6 cases of massive uterine hemorrhage from carcinoma of the cervix controlled by ligation of the hypogastric artery. In two of their operations, the ovarian vessels had to be ligated as well to control the bleeding. They advocated the transperitoneal approach to this procedure. They pointed out that if the hemorrhage is not controlled after hypogastric ligation, the ovarian vessels should be ligated. This can be accomplished by one abdominal incision using the transperitoneal approach to the hypogastric artery. They were not impressed with the danger of peritoneal contamination.

So far, we have dealt with the hypogastric ligation as it applies to malignancy. This procedure has valuable uses in benign diseases as illustrated by our cases 2 and 3.

The hypogastric artery may be ligated to control hemorrhage at the time of an operation. Severe hemorrhage may be encountered at the time of abdominal or vaginal hysterectomy if the uterine blood vessels should escape a ligature. Very often the blood vessels retract from view and out of the field, and it is difficult to find the bleeding source to control it. In the attempt to control the bleeding, clamps may be placed on many structures without getting to the actual source of the bleeding. In this process there

may be damage to the ureters as well as to the surrounding tissues.

Phaneuf[12] states that when the uterine artery is lost at the time of vaginal hysterectomy, the safest way to control hemorrhage is to make an abdominal incision and ligate the hypogastric artery on the side involved. Phaneuf's principle can also be applied to abdominal hysterectomy under similar circumstances. If the uterine artery retracts, it is a simple and safe procedure to place a pack at the site of bleeding and open the posterior parietal peritoneum over the bifurcation of the common iliac vessels and ligate the hypogastric. In this way ureteral injuries may be avoided, and one may proceed with the operation without fear of great blood loss and the shock that would result.

We have recently employed this principle in the following case:

M. D., age 38, was admitted to the Baroness Erlanger Hospital on March 14, 1959, because of severe abdominal pain.

Examination at that time revealed a negro woman in moderate discomfort; blood pressure and pulse were within normal range. The abdomen was consistent with an 8 months gestation, fetal heart tones were heard in the left lower quadrant. Because of the severity of the abdominal pain, an x-ray study was ordered which showed a fetus to be in a peculiar position lying completely on the left side of the abdomen. There was extension of the legs rather than the usual fetal posture. The vertex was presenting and entering toward the pelvis. All laboratory tests at that time were within normal limits and no change was noted.

The diagnosis of abdominal pregnancy or pregnancy within a double uterus was entertained. Because of the prematurity of the fetus, it was decided to wait before any procedure was done to observe the patient's reaction and allow greater maturity of the fetus. After 5 days in the hospital the pain subsided and the patient was discharged. She was not seen again until April 11, 1959, when she stated that after going home her pain returned but was not severe enough to bring her to the doctor's office. During the past week it had gradually grown more severe and she had no longer felt fetal motion.

Blood pressure, pulse and laboratory findings were within normal limits at this time, examination showed extreme tenderness over the abdominal wall particularly on the left side with slight edema of the skin over the anterior abdominal wall. No fetal heart tones were heard. X-ray examination again revealed the peculiar position of the fetus but there was angulation of the spine consistent with fetal death.

A laparotomy was performed and on opening the abdominal cavity it was found that we were dealing with an abdominal pregnancy. A stillborn fetus approximately term size was delivered. After delivery of the fetus, examination further revealed that the pregnancy had been confined within the leaves of the right broad ligament and had twisted around posterior to the uterus to present itself on the left side as was shown on the x-ray film. After removal of the fetus the placenta was found attached to the base of the broad ligament. The upper pole of the placenta extending to the incision had separated and there was a large amount of bleeding coming from this area. To control this bleeding blood vessels supplying this area, which apparently had come from the infundibulopelvic ligament, were ligated. This did not control the bleeding and pressure was made over the bleeding site of the placenta. The posterior parietal peritoneum over the right external iliac artery was palpated and the peritoneum opened and dissected until the bifurcation of the common iliac artery was found. The hypogastric artery on the right side was ligated with immediate cession of bleeding.

With bleeding under control it was found that the placenta and the uterus could be removed in a block without difficulty. This was done and the patient's postoperative course was completely uneventful. She was discharged on her 9th postoperative day. Total blood replacement was 1,500 cc.

Kirschbaum[13] reported a case requiring hypogastric artery ligation bilaterally to control oozing from the broad ligament following operation for ectopic pregnancy. In this case all anatomic landmarks were lost and bleeding was uncontrollable by other means. The hypogastric blood vessels were ligated on both sides and the bleeding controlled, an interesting side note being the fact that the patient was able to retain her uterus.

All of us have been faced with the problem of postoperative hemorrhage following total abdominal hysterectomy. This bleeding usually comes from the angles of the vaginal vault. It is most frequently controlled with simple packing, or ligation when the exact bleeding point can be found. In a small number of cases these conservative procedures may not be sufficient, and the bleeding will continue. It may require reopening the abdomen and ligating the bleeding point, but the tissues in the area of the operative site are extremely friable and religation of the bleeding point at times is impossible because the stumps of the blood vessels are necrotic and friable, and when clamped will break away.

In several documented reports by Kirschbaum,[13] Decker,[14] Hecht and Blumenthal,[15] the bilateral hypogastric ligation had to be used to control such postoperative hemorrhage following abdominal hysterectomy. In one case, bleeding started on the eighteenth postoperative day and was controlled by re-

suturing the vaginal vault and vaginal packing.[15] Bleeding occurred again on the twenty-seventh postoperative day and packing controlled the bleeding temporarily. The vaginal vault was again inspected and bleeding noted to be coming from the left side of the vaginal vault, but could not be reached. The hypogastric vessels were eventually ligated, but before this was done the patient was in shock on 3 occasions and had received a large number of blood transfusions. The lesson to be learned from the experience of these men indicates that there is a definite place for hypogastric ligation in controlling the postoperative hemorrhage. Their experiences, as well as ours, suggest the following procedures to be used under such instances:

1. Control of bleeding by packing the vaginal vault.

2. Ligation of the bleeding point in the vaginal vault if technically possible.

3. However, if the first two procedures are not effective and bleeding continues, ligation of the hypogastric artery should be done, unilaterally or bilaterally, through an abdominal incision.

All authors quoted so far have been impressed with the simplicity of hypogastric ligation, as well as the lack of complications related to the bladder, rectum and anus. It is impossible to evaluate how many times the hypogastric artery has been ligated. Hecht and Blumenthal[15] stated that subsequent to their experience, they had ligated a hypogastric artery on six or more occasions during the course of radical hysterectomy for carcinoma of the cervix, and are not impressed by any adverse effects.

Falk[16] feels that hypogastric artery ligation is indicated at times to control severe hemorrhage, and does not feel that there should be any concern about vascular depletion to the bladder, pelvic ureter, or anus. (He has made studies of the hypogastric circulation in autopsy specimens, using radiopaque media, and demonstrated the extensive collateral circulation.)

Notwithstanding, Tajes[1] reported a case of abdominal perineal resection in a 58 year old woman in whom he ligated the hypogastric artery during the operation. The patient subsequently developed necrosis of the buttocks in the areas supplied by the inferior and superior gluteal arteries. He also described two other case reports by Finaly[17] in which there was evidence of necrosis of the bladder following ligation of the hypogastric artery during a surgical procedure. Tajes[18] believes these complications are extremely rare, and has only found two other reports besides his own in literature. He also believes one should not be afraid to use this procedure when indicated.

The technic is quite simple if the anatomic landmarks are present. It may be done simply by opening the posterior parietal peritoneum over the promontory of the sacrum. The hypogastric artery is easily found by dissecting laterally until the bifurcation of the common iliac artery is located. If possible, the ureteral branches of the hypogastric artery should be identified, and the hypogastric artery should be carefully dissected from the internal iliac vein. After this dissection the artery may be ligated distal to the ureteral branch. If the ureteral branch is not readily identifiable, the hypogastric artery may be ligated just below its origin from the common iliac artery.

If anatomic landmarks are difficult to recognize because of distortion due to adhesions, poor anesthesia, or postoperative derangement of the pelvis, the technic can be modified as follows:

1. The pulsations of the external iliac artery are palpated.

2. An incision is made through the peritoneum on the superior border of the external iliac vessel, and the vessel is traced along its course until the bifurcation is found.

3. The hypogastric artery is carefully dissected away from the underlying internal iliac vein. Care at this point is necessary to prevent injury to the vein.

4. The hypogastric artery can then be doubly ligated using silk, cotton, or chromic catgut.

5. Ligature may be facilitated with an aneurysm needle or simply by passing a Kelly clamp behind the artery, and having the assistant pass the ligature down to the open jaws of the clamp.

Summary

1. Four cases of severe hemorrhage requiring ligation of the hypogastric artery to control bleeding have been reported.

2. The collateral circulation of the hypogastric artery has been reviewed and found to be adequate after ligation.

3. The experiences of other operators with ligation of the hypogastric artery have been summarized, and hypogastric artery ligation has been found to have a definite place in gynecology under the following circumstances: (a) uncontrollable bleeding from carcinoma of the cervix or endometrium; (b) severe hemorrhage at the time of pelvic surgery; and (c) the control of postoperative bleeding following pelvic operations.

References

1. Tajes, R. Venancio: Ligation of the Hypogastric Arteries, Its Complications in Resection of Cancer of the Rectum, Am. J. Gastroenterol. 26:612, 1956.
2. Bastiaanse, Van Bouwdiyk: Personal communication.
3. Alfieri, E.: Carcinoma Cervicale Con Vasta Invasione Delle Ghiandole Pelviche, Operato Col Metodo Del Wertheim Previa Allacciatura Delle Arterie Ipogastriche, Atti Soc. Ital. Ostet. 36:50, 1940.
4. Asteriades, Tasso: Des Ligatures Atrophiantes Comme Traitement Palliatif Des Cancers Inoperables De L'uterus, Gynec. et. obst. 10:25, 1924.
5. Fredet, P.: Ligature De L'artere Iliaque Interne Et Ligature De L'artere Uterine Dans Le Cancer Inoperable De L'uterus, Bull. Soc. anat. 73:181, 1898.
6. Green-Armytage, V. B.: Ligation of the Internal Iliac and Ovarian Arteries for Inoperable Carcinoma of the Uterus, Combined with Curettage and Cautery, Indian M. Gaz. 48:270, 1913.
7. Taylor, H. C., and Peightal, T. C.: End Results Obtained in a Series of Two Hundred and One Cases of Carcinoma of the Cervix, Am. J. Obst. & Gynec. 8:288, 1924.
8. Kelly, Howard: Ligation of Both Internal Iliac Arteries for Hemorrhage in Hysterectomy for Carcinoma Uteri, Bull. Johns Hopkins Hosp. 5:53, 1894.
9. Leventhal, M. L., Lash, A. F., Grossman, A.: Hemorrhage from Carcinoma of Cervix; Control by Extraperitoneal Ligation of Hypogastric Arteries, Surg. Gynec. & Obst. 67: 102, 1938.
10. Greenhill, J. P.: Surgical Gynecology. 2nd ed. Chicago, Year Book Publishers, 1957.
11. Salzberg, A. M., Fuller, W. A., and Hoge, R. H.: The Surgical Management of Profuse Hemorrhage from Uterine Carcinoma, Surg. Gynec. & Obst. 97:773, 1953.
12. Phaneuf, Louis E.: Accidents Complicating Pelvic Surgery in Women, New England J. Med. 247:39, 1952.
13. Kirschbaum, Harry: Ligation of Internal Iliacs for Uncontrollable Pelvic Hemorrhage, Urol. & Cutan. Rev. 54:72, 1950.
14. Decker, Wayne H.: Ligation of the Hypogastric Artery in Post-operative Uterine Artery Hemorrhage, Obst. & Gynec. 5:109, 1955.
15. Hecht, E. L., and Blumenthal, E. D.: Recurrent Bleeding from the Vaginal Vault Following Total Abdominal Hysterectomy, Am. J. Obst. & Gynec. 67:195, 1954.
16. Falk, Henry C.: Personal communication.
17. Finaly, R.: Quoted by Tajes, R. Venancio.
18. Tajes, R. Venancio: Personal correspondence.

Discussion (Abstract)

Dr. Arthur L. Haskins, Baltimore, Md. Drs. Binder and Mitchell have indicated that hemorrhage from the female reproductive tract remains a problem in clinical obstetrics and gynecology. They have approached the solution to this problem through surgery, and specifically through ligation of the hypogastric (internal iliac) artery which provides the major blood supply to the reproductive tract and adjacent tissues.

The hypogastric artery has two major divisions. The posterior division of the hypogastric artery is of relatively little importance in this study, since it provides only parietal flow through the iliolumbar, lateral sacral and superior gluteal arteries. It is the anterior branch which gives rise to the obturator, inferior gluteal, internal pudendal, the superior vesicle, middle hemorrhoidal, uterine and vaginal arteries from which the major hemorrhage from the female reproductive tract occurs.

Collateral circulation of the tissues applied by the hypogastric system is extensive in most areas. The perineum and urinary bladder, however, receive minimal extra-hypogastric collateral circulation.

It is apparent from the presentation of Drs. Binder and Mitchell that ligation of the hypogastric artery does curtail hemorrhage and does not induce tissue changes secondary to ischemia of the area involved. Ligation of the hypogastric artery in the presence of intractable hemorrhage is apparently a safe and effective means of inducing hemostasis.

Having established the safety and effectiveness of the procedure, it then becomes important to establish the indications for the procedure. In reviewing the case reports presented by the authors, we find that in case 1, the patient had an inadequately treated carcinoma of the cervix and severe vaginal hemorrhage. Hemostasis was obtained by hypogastric ligation, a valid indication for the procedure. Its effectiveness was proven by the subsequent clinical course. There is, however, some question concerning the statement relative to the follow-up examination which "revealed a rectovaginal fistula attributable to radiation necrosis and not to deprivation of blood supply by artery ligation." Since radiation necrosis is basically due to ischemia, the statement that the necrosis is due to ischemia by radiation and not due to artery ligation would be somewhat difficult to prove. A critical observer must ask the question as to whether the formation of the rectovaginal fistula might not have been due, at least in part, to the ligation of the hypogastric artery. In case 2, a 42 year old grandmultipara with ruptured membranes was subjected to a Pitocin induction. Following this questionable procedure, rupture of the uterus and laceration of the vaginal vault and broad ligament occurred. Bleeding was controlled from the involved side by ligation of the hypogastric artery. The chief indication for this ligation was technical, since the right uterine artery could not be ligated separately. This is undoubtedly a satisfactory indication for this surgical procedure. In case 3, a 33 year old, para 3, the premature separation of the normally implanted placenta occurred in association with toxemia and chronic renal disease. This patient was subjected to hysterectomy in the presence of an obvious coagulation defect. Admittedly, the bleeding was controlled at the time of ligation of the right hypogastric artery. One cannot help but wonder, however, whether the hysterectomy in itself was indicated in the presence of a clotting defect. If the indication for hysterectomy was present, the second note of conjecture has to do with the last paragraph in which it is revealed that the patient received 10,000 ml. of whole blood and 12 grams of fibrinogen. It is quite possible that this replacement therapy could have produced the hemostasis without hypogastric artery ligation. The fourth case presented is that of a 38 year old patient with a full term abdominal pregnancy. In the process of removing the fetus the placenta separated in part, bringing about intractable hemorrhage in the area of the right broad ligament.

Because of this, hypogastric ligation on the right side was carried out with immediate cessation of bleeding. This is another reasonable indication for this ligation procedure.

In summary, the authors consider that hypogastric artery ligation has a definite place in gynecology. The indications are the presence of uncontrolled bleeding from carcinoma of the cervix or endometrium, severe hemorrhage at the time of operation and the control of postoperative bleeding. These indications are certainly ones which are valid for hypogastric ligation.

It is quite possible, however, that routine ligation of the hypogastric arteries in the radical hysterectomy associated with the Taussig type of node dissection might well be the major indication for hypogastric artery ligation. This provides an improved technical approach to the radical hysterectomy.

The authors should be commended for emphasizing the application of basic anatomic knowledge to clinical problems. They have reviewed previous contributions to gynecologic surgery in this regard. They have suitably illustrated their points with case histories. It has been a pleasure and privilege to review their contribution.

Fifty-fourth Annual Meeting

Southern Medical Association

St. Louis, Mo., Oct. 31-Nov. 3, 1960

Evaluation of Diagnostic Procedures in the Clinical Diagnosis of Gastric Cancer*

M. FRANK SOHMER, M.D., DAVID CAYER, M.D., and ZELMA A. KALNINS, M.D.,† *Winston-Salem, N. C.*

Gastric cancer is notoriously difficult of diagnosis. Many studies have been made in searching for methods of early diagnosis. The present study evaluates these several means of investigations as to accuracy and contributions to early diagnosis.

CANCER OF THE STOMACH accounted for 5.6% of the cases of cancer reported in 1956. Of the 24,000 males and 12,500 females found to have gastric cancer during this year, 90% died.

Screening Procedures for the Detection of Gastric Cancer

Early detection of gastric cancer is not possible through the history and physical examination alone. The few symptoms of early cancer are usually atypical or mild, and diagnostic physical findings are invariably associated with advanced, incurable disease. The incidence of gastric cancer is highest in men after the age of 45, and in women after 50; it is greatly increased in individuals with achlorhydria, pernicious anemia, atrophic gastritis, and gastric polyps. Periodic observation and re-evaluation of persons with any of these conditions are essential prophylactic measures. While individuals with type A blood are apparently more prone to gastric cancer than those in other blood groups, the increase in incidence is not great enough to warrant periodic observation.

Determination of gastric acidity. Determinations of gastric acidity provide a valuable screening test. Probably more than 50% of the patients with gastric cancer are achlorhydric even after histamine stimulation, and as many as 90% may have *hypo*chlorhydria. Hitchcock[1] has estimated that the incidence of gastric cancer in patients with achlorhydria or hypochlorhydria is more than 5 times greater than that in patients with normal acidity. Routine gastric analysis offers a practical means of detecting this abnormality with minimal expense. The development of ion exchange technic for determining gastric acidity without intubation should permit more widespread application of this valuable screening procedure.

Roentgen surveys. Mass roentgen surveys have been undertaken in selected groups. In one series of 2,500 patients, only 323 of whom were below the age of 40, the use of photofluorography revealed 18 cases of probable gastric malignancy.[2] Only 3 of these patients, however, were without complaints or physical findings which might have suggested the presence of gastric cancer. A statistical study on the incidence of gastric cancer in the population past the age of 40 indicates that not more than 3 persons per thousand would have the disease at any one time.[3] In view of the amount of work involved, the time required of highly trained personnel, the potential dangers of excessive radiation through repeated examinations, and the number of resectable lesions found, routine roentgen examination of the stomach in asymptomatic persons does not appear justified except in the presence of achlorhydria or one of the predisposing conditions mentioned above—pernicious anemia, atrophic gastritis, and gastric polyps.

*Read before the Section on Gastroenterology, Southern Medical Association, Fifty-Third Annual Meeting, Atlanta, Ga., November 16-19, 1959.

†From the Departments of Medicine and Pathology of the Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, N. C., and the Cytology Section, Field Investigations and Demonstrations Branch, National Cancer Institute, National Institutes of Health, United States Public Health Service, Bethesda, Md.

Gastroscopy. Even though gastroscopy is performed on a large scale, it obviously is not a routine procedure. Patients are often reluctant to submit to gastroscopy unless the indication is specific. The diagnostic accuracy of gastroscopy is limited by the fact that it is impossible to visualize certain areas of the stomach, to obtain biopsies under direct visual control, or to identify correctly the nature of all lesions by inspection alone. Gastroscopy is of value primarily in making possible an unequivocal diagnosis of gastritis and in disclosing occasional lesions not shown by roentgen studies. It also permits more accurate diagnosis of lesions found on x-ray examination, and makes it possible to observe the effects of treatment on gastric ulcerations of uncertain etiology.

Cytology. Gastric lavage, followed by cytologic study of the gastric contents, may disclose the presence of malignant cells before a lesion could be detected by roentgenologic or gastroscopic examination. This method, however, is a time consuming procedure requiring highly specialized technical assistance. Interpretation of gastric cytology is considerably more difficult than the routine study of cervical smears.

Exfoliation of gastric cells is a normal physiologic process. Malignant cells, because of friability and necrosis, lack of adhesiveness, and greater susceptibility to trauma, have an increased tendency to exfoliation. A variety of methods for obtaining gastric cells have been described. These include:

1. Technics for mechanical removal (gastric balloon, brush).

2. Mucolytic agents (papain, chymotrypsin).

3. Simple gastric lavage with saline, Ringer's or buffered solution, using forceful injection of fluid with multiple aspirations and reinjections.

The mechanical methods appear of particular value when a lesion in the antrum or fundus is suspected, or when simple lavage has proved unsatisfactory. Sheets of cells are usually obtained by mechanical abrasion, but the time required and the occasional untoward effects of passing balloons and brushes have discouraged the widespread use of these procedures. Although attempts to liquefy the mucous layer in the stomach with crude enzyme mixtures do not regularly yield well-preserved cells, some investigators have reported favorably on the use of crystallized chymotrypsin.[4] Saline lavage and aspiration, the technic we have used, is the simplest and least traumatic procedure. In most instances adequately preserved cells are recovered in sufficient quantity to permit diagnostic evaluation.[5]

A review of the literature indicates that, while gastric cytology is a highly accurate diagnostic procedure, its routine use yields no better results in the early diagnosis of cancer than does radiology or gastroscopy. It is possible, however, that in patients with chronic gastritis, pernicious anemia, or polyps of the stomach routine cytologic studies might permit the detection of early malignancy before invasion or metastatic growth has occurred. Since gastric cytology may also provide confirmatory evidence of cancer when other diagnostic tests are equivocal, it is a most useful ally in the diagnosis of gastric cancer.

Other tests. A variety of other procedures, including determinations of plasma pepsinogen and levels of serum and gastric lactic dehydrogenase, other enzyme studies, and bone marrow examinations, usually add little to the studies already mentioned. Such technics as study of the peripheral blood for malignant cells and various serologic tests for cancer are still in the investigative or developmental stage, and are available only in larger research centers.

Clinical Study of 300 Patients with Gastrointestinal Complaints

Selection of patients. In the study to be reported, various methods of examination have been employed in a group of 300 patients, selected because of symptoms referable to the gastrointestinal tract or findings which suggested gastric cancer. Cases of proven duodenal ulcer were excluded. The group included 181 men whose ages averaged 54.4 years, and 119 women with an average age of 54.8 years. All of the patients had, on one or more occasions, gastric analyses, roentgen studies of the upper gastrointestinal tract, and gastric lavage. Gastroscopic examinations were performed in 18 of the 66 patients in whom roentgen or cytologic abnormalities were found.

TABLE 1

RESULTS OF DIAGNOSTIC TESTS IN 4 PATIENTS WITH SARCOMA OR LYMPHOMA

Cytology		Number of	Acid	X-ray Diagnosis		
Preoperative	Postoperative	Cases	Present	Benign	Malignant	Final Diagnosis
2	1	1	1	1		Hodgkin's
2		1	0	1		Lymphosarcoma
	2	1	1		1	Reticulum cell sarcoma
2	No surgery	1	1		1	Hodgkin's

Gastroscopy was performed on one patient and showed diffuse nodular involvement with hemorrhagic areas.

Findings in 4 patients with sarcoma or lymphoma (Table 1). Lymphosarcoma was diagnosed by surgical biopsy or at autopsy in 4 patients. Three of these had free acid in the stomach. In 3 patients the roentgen studies indicated abnormalities: a gastric mass in one, hyperatrophic rugae in another, and in the third an ulcer on the lesser curvature. Diffuse gastric involvement, with nodulation and hemorrhagic areas, was noted in the one patient examined by gastroscopy.

In all 3 patients studied before operation, cytologic examinations of gastric washings were negative (Class 1 or 2*). Surgical exploration revealed infiltrating submucosal lymphosarcoma in 2 patients. Since the gastric mucosa in both cases was uninvolved and intact, it is not surprising that both preoperative and postoperative cytologic examinations were negative. In the patient whose x-ray studies were also negative, postmortem examination revealed a Hodgkin's sarcoma. The gastrointestinal tract was not involved, although gastrointestinal symptoms had been present.

The remaining patient was not studied cytologically prior to a gastric resection for a recurrent ulcer on the lesser curvature. At operation reticulum sarcoma cells were found in the borders of the ulcer. Cytologic examination of the gastric washings 6 months later, when the patient was asymptomatic, revealed cells resembling reticulo-endothelial cells, but showing no features diagnostic of malignancy. The presence of these cells was taken as an indication that the lesion had recurred, and roentgen therapy was administered despite the patient's lack of symptoms and a negative radiologic examination of the stomach.

Although conclusions drawn from such a small group of patients may not be valid, certain observations can be made. It would appear that roentgen examination and gastroscopy may be more valuable than cytologic study in the diagnosis of infiltrating submucosal gastric tumors such as lymphosarcomas. Experience with 2 of the patients in this group would suggest that individual lymphoma or reticulum cells may be interpreted as normal.

Findings in 25 patients with benign gastric ulcers (Table 2). Twenty-three of the 25 patients in this group had free hydrochloric acid demonstrated on routine gastric analysis.

In 8 patients, the radiographic appearance of the lesion strongly suggested malignancy—a diagnosis which was subsequently disproved in 7 patients. In the eighth case no follow-up study was available.

*The cytologic specimens were classified as follows:
Class 0—inadequate for diagnosis.
Class 1—no atypical or abnormal cells.
Class 2—atypical cells, but no evidence of malignancy.
Class 3—cells suggestive of malignancy, but not conclusive.
Class 4—cells strongly suggestive of malignancy.
Class 5—malignant cells.

TABLE 2

RESULTS OF DIAGNOSTIC TESTS IN 25 PATIENTS WITH BENIGN GASTRIC ULCERS

Cytology	Number of Cases	Acid Present	X-ray Diagnosis		Final Diagnosis	
			Benign	Malignant	Benign	Malignant
0	1	1	0	1	1	0
1	10	10	10	0	10	0
2	10	9	6	4	9*	0
3, 2	2	1	1	1	2	0
3	2	2	0	2	2	0

Gastroscopy was performed on 10 patients, with visualization of the lesion in 7; the ulcers were considered benign in 6 cases, malignant in one.

*In the tenth patient follow-up studies were not obtained.

Ten patients in this group were studied by gastroscopy. In 6 of the 7 cases in which the lesion was visualized, it was considered benign; in the seventh case a gastroscopic diagnosis of malignancy was subsequently disproved.

In one patient the specimen obtained by gastric lavage was classified as inadequate for cytologic diagnosis (Class 0). This patient had pyloric obstruction, with retention of food and secretions. Necrotic debris in the ulcer itself, inflammatory cells, and retention of secretions contributed to the failure to obtain a satisfactory specimen. The lesion found at operation was benign.

Four patients had initial cytologic specimens suggestive of malignancy (Class 3). In 2 patients, however, subsequent examinations were interpreted as Class 2, and both were removed from the group classified as possibly malignant. One of these patients later had a subtotal gastric resection because of the repeated absence of free hydrochloric acid after histamine stimulation and failure of the lesion to heal after 2 weeks of therapy; the cytologic diagnosis of benignancy was confirmed by pathologic study of the resected lesion. A second x-ray examination of the other patient after 2 weeks of therapy showed healing of his ulcer; 3 months later, follow-up roentgenologic and cytologic examinations were normal.

In a third patient, radiologic examination was suggestive of a malignant ulcer of the greater curvature, and only one cytologic examination was made prior to operation; this was graded as Class 3. Since laparotomy revealed only diffuse gastric bleeding without ulceration, a resection was not done. This patient gradually improved and had had no recurrence of his symptoms.

In the remaining patient with Class 3 cytology, the roentgen interpretation was retrogastric mass with fixation, an abnormal mucosal pattern, and a possible ulcer on the greater curvature. At operation subacute gastritis and superficial erosion of the mucosa were found.

In the remaining 20 patients the clinical impression of benignancy was confirmed by the cytologic findings (Class 1 or 2), and in all of these healing was indicated by follow-up studies, or the benign nature of the lesion was confirmed at operation.

These 25 cases indicate the value of gastric cytology in the differential diagnosis of ulcerating gastric lesions. Although specimens suggestive of malignancy were obtained in the initial study of 4 cases which were subsequently proved to be benign, there were no false negatives. If a patient with a gastric ulcer has a negative cytologic specimen (Class 1 or 2) and free hydrochloric acid, it may be assumed that his lesion is benign. Because atypical cells are often present during the healing phase of benign gastric ulcer, a cytologic examination which falls in Class 3 should be repeated and interpreted in the light of other clinical findings. Class 4 cytology, however, should have the diagnostic implication of a positive surgical biopsy.

Findings in 22 patients with gastric cancer (Table 3). The diagnosis of gastric cancer was made in 22 patients. In 14 the diagnosis was confirmed by laparotomy. In the remaining patients, the diagnosis was substantiated by the subsequent course or by evidence of metastases associated with the gastric lesion.

Free hydrochloric acid was present in 12 patients—jut over half the group. In 19 the clinical diagnosis of malignancy was suggested by the radiologic examination, but in 3 patients the location and benign radiologic appearance of the defect led to the initial diag-

TABLE 3

RESULTS OF DIAGNOSTIC TESTS IN 20 PATIENTS WITH GASTRIC CANCER

Cytology	Number of Cases	Acid Present	X-ray Diagnosis		Final Diagnosis	
			Benign	Malignant	Benign	Malignant
0	3	2	1	2		3
1	0					0
2	1			1		1
3	10	5	2	8		10
4	7	4		7		7
5	1	1		1		1

Gastroscopy was performed on 4 patients, with visualization of the lesion in 3. Two lesions were diagnosed as malignant, one as probably malignant.

nosis of a benign lesion. Gastroscopic examination, performed on 4 patients, led to a diagnosis of malignancy in 2 cases and of probable malignancy in one. In the fourth case a malignant ulcer high on the lesser curvature was not visualized.

The results of cytologic examination in these 22 patients are shown in table 3. In 3 cases satisfactory specimens of the gastric contents were not obtained. In one patient a cytologic examination made preoperatively was reported as Class 2—a false negative. A second examination 6 months after resection showed cells suggestive of malignancy (Class 3). This patient had a linitis plastica type of infiltrative mucinous adenocarcinoma, which did not involve the surface layers of the gastric mucosa. It is conceivable that abrasive technics of gastric lavage might have permitted the diagnosis to be made preoperatively in this case. In one patient gastric washings obtained 16 months after gastric resection for cancer showed malignant columnar epithelial cells (Class 4). This patient was asymptomatic at the time.

All of the studies performed in this group of patients with cancer proved helpful, and the variety of procedures resulted in a high degree of diagnostic accuracy.

Findings in 15 patients with miscellaneous roentgen abnormalities of the stomach (Table 4). Seven patients with *prepyloric ulcers* were studied. All had free hydrochloric acid, and the gastric washings from each were reported in cytologic Class 1 or 2. Follow-up studies confirmed the clinical impression of benignancy in each case.

Roentgen abnormalities consisting of gastric narrowing, deformity, or filling defects were found in 8 additional patients. In only one of these were cytologic studies abnormal. This patient is a 39 year old woman with a past history of hematemesis, gastric resection, and gastroenterostomy. Although two cytologic examinations of the gastric contents have been interpreted as Class 3, no evidence of malignancy has appeared in this patient after 9 months of follow-up.

In 3 patients the final diagnosis of *pancreatic cancer* was confirmed at operation or at autopsy. In each of these 3 cases the preliminary diagnosis was gastric cancer, but the gastric cytology was Class 2. The finding of a normal gastric cytology should always suggest the possibility that such radiologic abnormalities in the stomach may be due to pressure defects or invasion by a lesion in the pancreas.

In one patient, benign gastric polyps were removed at operation. In the others with abnormal roentgen findings in the stomach, adequate intervals of follow-up and subsequent studies have failed to reveal malignancy.

Summary

1. Gastric analyses, barium studies of the upper digestive tract, and cytologic studies of gastric washings were made in 300 patients with digestive symptoms or findings suggestive of gastric lesions. Gastroscopic examinations were performed in 18 of 66 patients in whom radiologic or cytologic abnormalities were found.

2. X-ray examination and gastroscopy ap-

TABLE 4

RESULTS OF DIAGNOSTIC TESTS IN 15 PATIENTS WITH MISCELLANEOUS ROENTGEN ABNORMALITIES OF THE STOMACH

X-ray Diagnosis	*Final Diagnosis*	*Number of Cases*	*Acid Present*	*Cytology*	*Comment*
Benign prepyloric ulcer	Same	7	7	1 or 2	All healed
Filling defect on the lesser curvature; gastric polyps; gastric cancer	Pancreatic cancer	3	3	1 or 2	
Atrial narrowing	? Gastric cancer	1	1	2	Repeat x-rays normal
Gastric polyps	Same	1	1	2	Benign polyps removed
Irregularity of the lesser curvature	Anxiety; healed ulcer scar	1	1	1	
? Linitis plastica	Gastric cancer	1	0	1	Atrophic gastritis
Gastroenterostomy	Anxiety	1	0	3, 3	History of hematemesis with 2 year follow-up

peared to be the most valuable diagnostic procedures in the 4 cases of sarcomatous gastric lesions. The cytologic findings were of no diagnostic value in 2 patients whose lymphomas had produced infiltrative, nonulcerating submucosal gastric tumors.

3. Twenty-three of 25 patients with benign gastric ulcers had free hydrochloric acid. Roentgen studies were considered suggestive of malignancy in 8 of these cases. Two patients had gastric washings graded as Class 3.

4. Free hydrochloric acid was present in only 12 of 22 patients with proven gastric cancer. X-ray examinations in this group of patients were considered as diagnostic or highly suggestive of cancer in 19 cases. A gastroscopic diagnosis of malignancy was made in 3 of 4 patients on whom this procedure was performed; one malignant lesion was not visualized. Eighteen patients in this group had cytologic specimens classified as 3, 4 or 5. In 2 patients, asymptomatic following resections for gastric cancer, cytologic examinations 6 and 16 months after operation indicate recurrence of malignant lesions.

5. In a group of 15 patients with miscellaneous roentgen abnormalities of the stomach, 13 were found to have free hydrochloric acid. In only one patient were the cytologic studies suggestive of malignancy (Class 3). Gastric cancer was suggested by the x-ray findings in 3 patients with free acid and Class 1 or 2 cytology. In these 3 cases a primary pancreatic malignancy was found at operation or at autopsy.

Conclusion

At the present time, gastric analysis, roentgenography, gastroscopy, and cytologic studies of the gastric contents appear to be the most essential procedures in the diagnosis of gastric cancer. The x-ray and gastroscope are of greatest value in detecting submucosal infiltrating gastric tumors. Gastric cytology is a most valuable adjunct in the diagnosis of gastric cancer and in the differentiation of ulcerating gastric lesions. Routine postoperative cytologic study is also of value in indicating a recurrence of cancer in asymptomatic patients. The variety of approaches provided by these procedures affords a high degree of diagnostic accuracy.

References

1. Hitchcock, R., Sullivan, W., and Wangansteen, H.: The Value of Achlorhydria as a Screening Test for Gastric Cancer, Gastroenterology 29:621, 1955.
2. Roach, J. F., Sloan, R. D., and Morgan, R. H.: Detection of Gastric Carcinoma by Photofluorographic Methods, Am. J. Roentgenol. 67:68, 1952.
3. Rigler, L. B.: Roentgen Examination of the Stomach in Symptomless Persons, J.A.M.A. 137:1501, 1948.
4. Rubin, C. E., and Benditt, E. P.: A Simplified Technic Using Chymotrypsin Lavage for the Cytological Diagnosis of Gastric Cancer, Cancer 8:1157, 1955.
5. Schade, R. O. K.: A Critical Review of Gastric Cytology, Acta cytol. 3:7, 1959.

Drug Reactions: Report of 150 Cases*

MASON I. LOWANCE,† *Atlanta, Ga.*

MANY REPORTS on drug reactions appear in the literature, but they are still too few to keep the majority of doctors alert to the catastrophic effects medicines may produce. Allergists are more concerned with individual sensitivity than are specialists in other fields, though all who administer medicines should be constantly aware that "one man's meat may be another man's poison."

When the court orders a physician to pay a patient $75,000 for having failed to record and remember that this patient was allergic to penicillin, when another patient, failing to so inform his doctor, dies after an average dose of this drug, it is time that we give more attention to sharing our experiences.

It is not the purpose of this discussion to differentiate the various types of reactions, nor to classify the adverse responses to drugs. Charkes[1] has conveniently placed them in five categories: (1) idiosyncrasy, (2) extension of a therapeutic effect, (3) allergic reactions, (4) poisonous effect, and (5) intolerance. (Robbins Bulletin also attempts to classify them.)

There are several excellent papers on drug sensitivity. Evans[2] has reported on hypersensitivity to penicillin, and Prickman,[3] in his article on "Catastrophic Drug Reactions," warns "mark all records sensitive to . . . adequate tests for drug allergy do not exist." Rising[4] says, "The thoughtful physician will use drugs with the full realization that in doing so he is taking a calculated risk. . . . This is not to say that one should stubbornly deny his patients the benefit of medications that are not fully understood." I cite these papers in recognition of the splendid publications already in this field, but wish again to emphasize that this paper is concerned with drug reactions rather than their type. We wish to present these cases as evidence that the greatest caution needs to be exercised in the administering of drugs.

Shortly after the advent of penicillin I gave a 30 year old lady an intramuscular injection of penicillin and dismissed her from the office. Before reaching the elevator she began to feel peculiar and returned to the office with generalized urticaria, marked dyspnea and some cyanosis, presenting a most distressing picture. Five minims of epinephrine hypodermically and 2 minims of epinephrine in calcium gluconate, intravenously, afforded some relief, but it was only after several hours and more epinephrine that I felt secure in allowing her to leave the office. This frightening incident with penicillin, occurring so soon after its introduction, made me doubly careful in administering it later. This applies to any of the other possible offenders. And yet, as cautious as I have been, I am reporting to you today on 150 cases whom I am seeing currently and all of whom have had disturbing reactions to drugs. I might add that no attempt was made to comb our files for unusual records or rare experiences (Tables 1-3). Please note that no analysis of the possible significance of age or sex was attempted. Four reacted to more than one drug. Penicillin produced urticaria and sulfonamides produced asthma in the same patient. In another case the use of sulfonamide was followed by fever and stomatitis ulcers. Chlorpromazine caused urticaria and shock in one instance. The tetracyclines seemed to produce sudden acute diarrhea in two patients. Meprobamate and phenylbutazone caused thrombocytopenic purpura in one case. Two patients who were allergic to beestings also had reactions to penicillin (Table 4).

TABLE 1

AGE AND SEX OF PATIENTS STUDIED

Age (In Years)	*Number of Cases*	*Sex*	
		(M	*F)*
0-20	11	4	7
20-40	30	7	23
40 and over	109	41	68

*Read before the Section on Allergy, Southern Medical Association, Fifty-Third Annual Meeting, Atlanta, Ga., November 16-19, 1959.

†From the Lowance Clinic, Atlanta, Ga.

TABLE 2

REACTION OCCURRED AFTER ADMINISTRATION

1st dose	62
2nd dose	25
3rd dose or later	63

Note that there were more mild or moderate reactions than severe ones, though death did occur in 2 instances, one immediately following administration of the drug and the other from thrombocytopenic purpura (Table 5). In the first case, the patient came into our office because of cardiovascular disease and active bronchopneumonia. He was asked if he had been given penicillin previously; he answered that he had taken it and had experienced no difficulty. Unfortunately I gave him the penicillin and he died. The family later informed me that he had had a rather severe reaction to penicillin before, but that the doctor had advised them not to frighten him about it since he might need penicillin again and refuse it.

The duration of reactions varied markedly (Table 6). Tetanus antitoxin produced chronic urticaria in one patient which continued for 2 years,—the longest period in any of those studied. Some reactions may appear to have been minor, but were major to these patients (Table 7).

Of the 88 patients with no recorded treatment, many had used antihistaminics at home and had already taken these before reporting their reactions. More than one therapeutic measure was used in 18 cases (Table 8).

TABLE 3

DRUGS WHICH PRODUCED REACTIONS

Drugs	*Number of Reactions*
Penicillin	105
Sulfas—including Diamerazole	16
Equanil	11
Tetracyclines	10
Aspirin	8
Miltown	7
Thorazine	4
Tetanus antitoxin	4
Butazolidin	3
Iodine	3
Chloromycetin	1
Digitalis	1
Liver	1
Tetanus toxoid	1
Thyroid	1
Trilafon	1
Polio vaccine	0

TABLE 4

ALLERGIC DISORDERS KNOWN BEFORE THESE DRUG REACTIONS—(SOME MORE THAN ONE)

Hay fever	24
Asthma	11
Urticaria	10
Eczema	4
Bee-sting reactions	2
None	104

One patient had both hay fever and asthma.

TABLE 5

INTENSITY OF REACTIONS

Mild	50
Moderate	58
Severe	42

TABLE 6

DURATION OF REACTIONS

Minutes	5
Hours	91
Days	42
Many weeks and up to 2 years	12

TABLE 7

TYPE OF REACTIONS (SOME MULTIPLE)

Urticaria	117
Eczema	11
Asthma	6
Dizziness and tingling	4
Nausea	2
Diarrhea	2
Death (sudden)	1
Shock	1
Acute temperature elevation	1
Angioneurotic edema	1
Headache	1
Rhinitis	1
Stomatitis ulcers	1
Tachycardia	1
Agranulocytosis	1
Thrombocytopenic purpura (death)	1

TABLE 8

TREATMENT—(IN 18 CASES MORE THAN ONE MEASURE EMPLOYED)

Epinephrine	9
ACTH	15
Antihistaminics	43
Calcium gluconate	10
Cortisone	7
Ephedrine	3
Ointment	2
Oxygen	2
None	88
Epinephrine and ACTH	3
Epinephrine and calcium gluconate	4
ACTH and antihistaminics	7
Calcium gluconate and antihistaminics	5
Antihistaminics and cortisone	2

Each case included in this series of slides would make an interesting case report in itself if it could be presented in detail, but time permits only a very brief sketch of a few of the more dramatic.

Case Reports

Case V-694 (Miss F. R.) Tetanus toxoid was given this patient and in about 30 seconds there was generalized urticaria, dypsnea, some cyanosis, and tachycardia. She was given epinephrine 0.55 cc. (hypo), which was followed immediately by calcium gluconate containing 0.25 cc. of epinephrine, intravenously. Epinephrine was continued every few minutes for some time. The patient was symptom-free in about 2 hours.

Case R-540 (Mrs. S. L.) This patient was given aqueous penicillin, intramuscularly, and in one minute she had dypsnea, some cyanosis, and generalized urticaria. Repeated doses of epinephrine plus calcium gluconate, intravenously, resulted in complete relief within one hour.

Case GG-120 (Mrs. N. L. S.) Iron was taken orally by this patient and in about 5 hours urticaria occurred which lasted 2 or 3 days. Several iron preparations were subsequently tried with the same results in each instance.

Case V-596 (Mrs. A. L. C.) Inhalation of penicillin was used and within 24 hours the patient developed hemorrhagic stomatitis which persisted for several days but cleared without treatment.

Case EE-722 (Mrs. H. F. F.) This patient was known to be sensitive to penicillin since 1952. On March 5, 1957, chlorpromazine, 25 mg., was given because of nausea and vomiting. In a few minutes she had generalized urticaria, and then a shock-like reaction, the blood pressure falling from 170/100 to 90/40. Supportive measures were used, and in a few hours she had recovered from this reaction.

Case U-532 (Mr. V. Y.) The diagnosis here was depression. Sparine was given by psychiatrist in small doses. In about a week there was elevation of the temperature, tachycardia, hypotension and the white blood count dropped to 200, ranging from this to 1,550 for about 10 days. The patient was critically ill with an infected throat. The diagnosis was agranulocytosis. Another fatality was expected for several days but the patient finally recovered.

Case J-29 (Mrs. R. K.) For the diagnosis of arthritis, 200 mg. of phenylbutazone was given every 4 hours for one week, and then 100 mg. t.i.d. for 3 additional days. On the tenth day a generalized purpuric rash appeared which progressed to bullous-like areas on trunk and thighs. The patient became extremely nervous even after the omission of the drug. In 2 weeks the rash was gone except for brown spots at all bullous sites. The nervousness progressed to the point of extreme depression (probably aggravated by other factors), and shock therapy was necessary. The patient never returned to normal.

Case M-115 (B. T.) For the diagnosis of arthritis and tendonitis about the elbows, 40 tablets of phenylbutazone were given from Nov. 25, 1957, and again 36 tablets in March 1958. Nervousness, depression and weakness began in April and by July a few "blue spots" were noted, and more and more of these appeared until September when ecchymotic spots became generalized from head to feet. The platelets on Oct. 9, 1958, were 330,000, two weeks later they were 20,000, and decreased to essentially none. The diagnosis was *thrombocytopenic purpura*. Treatment with 60 to 80 mg. of prednisone daily was fairly satisfactory at first. Transfusions then became necessary. Bone marrow examinations and all other indicated laboratory studies were done but no helpful information was obtained. The patient's condition fluctuated and continued to remain critical although as much as 100 mg. of prednisolone was given daily. As a last resort we increased the dose, experimentally, to 400 and even 500 mg. daily. The platelet count quite promptly rose to 336,000, but the patient died of complications of his hemorrhagic state.

Conclusions

The above reactions occurring in any one's office would make one conscious of the dangers which may result from the drugs we prescribe. We should exercise caution both in the initial prescribing as well as in the quantity prescribed. This gives patients more security and certainly keeps one in closer touch with them and with their reactions to medications.

References

1. Charkes, N. David: Meprobamate Idiosyncrasy, A.M.A. Arch. Int. Med. 102:584, 1958.
2. Evans, E. C.: Hypersensitivity Reaction to Penicillin, J. M. A. Georgia 48:544, 1959.
3. Prickman, L. E.: Catastrophic Drug Reactions, Minnesota Med. 41:751, 1949.
4. Rising, J. D.: Medicine, Miracles and Mischief, Postgrad. Med. 24:200, 1958.

Tonography in Office Practice*

JOSEPH H. DERIVAUX, M.D., *Birmingham, Ala.*

The author discusses the place of tonography in the diagnosis of glaucoma, and as an aid in classification, prognosis, and choice of therapy.

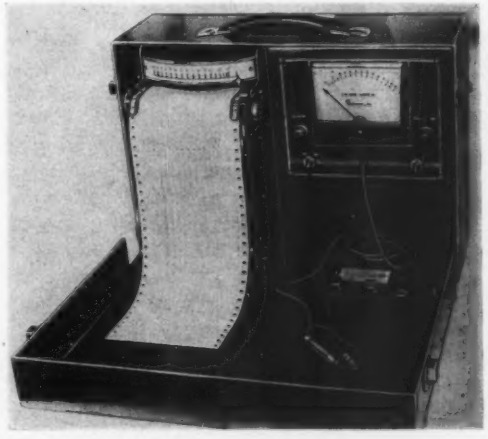
THAT TONOGRAPHY has become established as an invaluable technic for research in the fields of normal and disturbed dynamics of the aqueous humor is well recognized and undisputed. It will be the purpose of this paper to lend support to the increasing trend of incorporating tonography into office practice. It is generally conceded that ideally this technic should be available to every ophthalmologist in the diagnosis and management of glaucoma patients, but whether this procedure is performed in the office of the ophthalmologist or made available through consultations with large clinical centers will depend upon local and individual situations. Modern tonographic units designed for office use are now available (Fig. 1). These are compact, efficient, and are not financially prohibitive. With reasonable care they can be relied on to furnish information with valuable clinical application. It will be shown subsequently how tonography aids in the diagnosis of glaucoma, renders more sensitive provocative testing, helps classify the type of glaucoma being dealt with, evaluates how well the glaucoma patient is being controlled, and aids in the determination of which type of medical or surgical therapy is most likely to be of optimum benefit. In spite of these impressive clinical applications, it is not my intent to minimize the importance of other equally important technics in the diagnosis and management of glaucoma, such as ophthalmoscopy, gonioscopy, applanation tonometry, and visual field determination, to mention a few. There is as yet no substitute for a carefully taken history and a thorough clinical examination. Tonography, however, definitely merits a place in the evaluation of glaucoma, and will prove far more practical in the hands of most ophthalmologists than various alternate technics, such as the plotting of diurnal fluctuations of intraocular pressure at frequent intervals around the clock.

Application of Tonography

Tonography in simple terms records the rate of decline in intraocular pressure, occurring simultaneously with a reduction in ocular volume, when a known weight of a Schiøtz electronic tonometer rests on the eye for a period of time, usually four minutes. It enables one to calculate the facility of outflow of the eye, thus allowing one to estimate whether there is an obstruction in the drainage pathway for aqueous humor. It does not establish the location of such obstruction; for this determination gonioscopy and biomicroscopy with the slit lamp are essential. If obstruction to outflow is present, yet undetectable by these means, it is assumed to exist distal to the anterior chamber angle, i.e., in the trabecular meshwork, canal of Schlemm, aqueous veins, or episcleral veins. Tonography also permits one to calculate (indirectly) the rate of aqueous formation.

It is important to realize, however, that

FIG. 1



*Read before the Section on Ophthalmology and Otolaryngology, Southern Medical Association, Fifty-Third Annual Meeting, Atlanta, Ga., November 16-19, 1959.

neither tonography nor any other technic presently available, will reveal the individual susceptibility to elevated intraocular pressure that characterizes any specific optic nerve.[1] Hence the criteria for evaluating the existence and severity of the glaucomatous state must be based on an assumption that this susceptibility is not appreciably different from an average derived from statistical appraisal of vast numbers of cases.

Knowledge of the intraocular pressure and the facility of outflow affords one of the best means of separating the glaucoma population from the normal. In the normal eye the continual secretion of aqueous humor by the ciliary body maintains an intraocular pressure of 10 to 25 mm. Hg., and this forces a constant outflow of aqueous (F) from the eye at a rate of approximately 2.3 cu. mm. per minute. This corresponds to a facility of outflow (C) of approximately 0.26, varying somewhat with age, and expressed as cu. mm. per min. per mm. pressure gradient.

When the initial intraocular pressure (Po) is higher than 20 mm. Hg. glaucoma should be suspected. When the facility of outflow (C) is less than 0.20 glaucoma is likewise suspected, and this suspicion becomes considerably heightened when the outflow facility is found to be less than 0.15. A convenient means of expressing both of these measurements is the Po/C ratio. Becker has shown that a Po/C ratio greater than 100 will characterize 71% of glaucoma cases, and only include 2% of the normal population. When combined with a provocative test of water drinking this becomes even more discriminative, detecting 97% of patients with glaucoma and including only 1% of the normal population.[2]

Secretion of aqueous by the ciliary body does not occur at a constant rate in normal nor glaucomatous eyes. It is a phasic phenomenon, and this diurnal fluctuation is usually exaggerated in glaucoma. When the ciliary body is "hyposecreting" the intraocular pressure may be sufficiently low to mask the glaucoma, but the impaired outflow facility as determined by tonography will oftentimes indicate the presence of a situation, which if substantiated clinically, e.g., by characteristic loss in visual field, can be termed "hyposecretion glaucoma." This is indicated by a flat tracing on the tonogram in the presence of relatively low intraocular pressure. At times this situation appears as a defense mechanism in glaucoma, an attempt, as it were, to offset the progressive deleterious effects of elevated intraocular pressure. This usually is only a transient phase and when discovered in patients with known or suspected glaucoma merits careful follow-up observation.[3]

On the other hand it is occasionally found that the outflow facility is normal even though the intraocular pressure is elevated. This is designated as "hypersecretion glaucoma" and is apt to be found in individuals, usually middle-aged women, with vasomotor and emotional instability. In such cases the tonogram will reveal an unusually steep slope.

It is of interest that the flat tonographic tracing found in "hyposecretion glaucoma" may be actually a case of "masked angle closure." A narrow angle can be converted to an open angle when one places a tonometer on the eye, and obviously gonioscopy is necessary to reveal the true causitive factor in such instances.[3]

When the basic disturbance is in the secretory mechanism, therapy should be directed to relieve this factor, as by the use of carbonic anhydrase inhibitors (which lower the rate of secretion approximately 50%) or by epinephrine-type of compounds (which lower the secretory rate an additive 30%). Surgical approach to lower the secretory rate may also be undertaken, viz., cyclodiathermy, cyclodialysis, or cycloelectrolysis.

When the primary disturbance involves an impaired outflow facility, one's therapy should be directed toward improving this faculty. Miotics are the classical drugs employed for this purpose, and the newer miotics (demecarium bromide [Humorsol] and echothiophate iodide [Phospholine]) are capable of increasing the outflow facility nearly 50 per cent. Interestingly enough, miosis is not necessary for the production of the pressure-lowering effect of these drugs, as proven by the fact that topical phenylephrine HCl (Neo-Synephrine) will reverse the miosis but not the beneficial effect on outflow and intraocular pressure.[3] Consequently, phenylephrine may be used to minimize some of the side effects of the powerful new miotics used in glaucoma therapy.

The outflow facility may also be increased

by surgery, viz., internal or external filtering procedures. The configuration of the angle of the anterior chamber, and the presence or absence of synechiae as determined by gonioscopy, will of course have a bearing on the choice of procedure, but tonography has also been found to be a useful means of deciding on the optimum surgical approach. A simple iridectomy is very unlikely to control the glaucoma if the outflow facility is less than 0.15, and in such cases an external fistulizing procedure such as an iridencleisis would be preferable.

Technic

The technic of tonography is not particularly difficult nor time consuming. Since the instrument requires about 30 minutes to "warm up," it is helpful to start the electrical current at the beginning of each day, to insure its being ready for use without delay. A voltage stabilizer is recommended to minimize sources of error that could be related to fluctuating potentials of electrical output. At least once a day a test graph is run with the aid of a micrometer gauge to correlate the scale readings on the tonometer dial with the scale units on the tonographic recording chart. Before each tonogram the tonographic unit is further standardized by precise adjustments at the "0" and "7" scale reading, while the tonometer is held on the test block. The tonometer plunger and barrel should be cleansed with lint-free tissue paper and distilled water before and after tonography of each eye, to insure complete freedom of the moving parts.

Each eye is anesthetized topically and the patient reclines in a comfortable position on the table with fixation being directed to a spot, preferably a light, on the ceiling. The patient's eyelids are gently separated and the tonometer footplate is centered on the cornea. It is expedient to hold the footplate off the cornea for 10 or more seconds, or else to wait a similar period with the footplate on the cornea, before commencing tonography. This minimizes the initial artifacts on the tonographic curve which are related to vasomotor reflexes, apprehension, and other sources. An appropriate tonometer weight is chosen to insure an initial scale reading of 3.0 units or more when the footplate is placed on the cornea. Tonography is usually carried out for 4 minutes on each eye, and this corresponds to 8 inches of recorded tracing.

The initial and final intraocular pressures are determined from tables which are calibrated for the appropriate tonometer weight used. The change in readings on the scale, corresponding to the fall in intraocular pressure during tonography, is readily calculated and this allows one to determine the facility of outflow from the same tables. For reasons previously mentioned it is also useful to calculate the Po/C ratio from these same data.

Besides the sources of error induced in tonography by the operator and the patient, there are inherent sources of error because some of the basic assumptions on which tonography is based are probably not entirely true. It is assumed, for instance, that during tonography the rate of inflow remains constant, that blood volume is unchanged, that episcleral venous pressure is not altered, that scleral rigidity remains the same, and that the outflow does not vary with fluctuations of the intraocular pressure. One must conclude that these sources of error must in some way be compensative because tonograms are remarkably reproducible, and the data derived therefrom is validated by comparison with other more elaborate technics. Measurements of aqueous flow by tonography compare with striking similarity to those derived from investigations based on turnover of chemical test substances, static chemistries, fluorescein appearance time, and perfusion studies.

Tonography renders provocative testing for glaucoma considerably more sensitive. When one is evaluating a case of possible glaucoma, the first step should be gonioscopy to investigate the anatomy of the anterior chamber angle.

In early angle closure glaucoma, before synechiae have formed, the intraocular pressure and outflow facility between attacks will usually be normal. If the chamber angle is narrow one should direct the provocative testing toward the embarrassment of that faculty by means of a dark room or mydratic provocative test, e.g., eucatropine HCl (Euphthalmine). If mydriasis results in an elevation of intraocular pressure above 10 units and/or a decrease in the facility of outflow as expressed in a Po/C ratio over 100, then glau-

coma will very likely be present. It will classically be of the "angle closure" type, and treatment, if correlative findings substantiate this, should be primarily surgical (e.g., iridectomy) to allow the aqueous better access through the anterior chamber angle.

When glaucoma is suspected in an eye with open anterior chamber angles, a provocative test of proven usefulness is the water drinking test, especially sensitive when combined with tonography. An elevation of intraocular tension and/or a decrease in the outflow facility as expressed by a Po/C ratio over 100 is probably the most sensitive test available to separate the glaucomatous population from the normal. Water drinking is thought to lower the outflow facility by "hydrating the trabecular meshwork," though the actual mechanism is still somewhat obscure.

It should be mentioned that water drinking is one of the factors which cause reduction in scleral rigidity. This entity is also known to be reduced in myopia, thyrotropic exophthalmos, and from miotics or ophthalmic surgery.[4] It is particularly important in these instances to correct tonography for variations of scleral rigidity. Applanation tonometry has the advantage of measuring intraocular pressure independently of the scleral rigidity factor, hence applanation measurements would be helpful in such cases.

The Friedenwald nomogram lends itself very nicely for plotting scleral rigidity.[4] The slope of the line demarcated by the applanation measurement and the electronic tonometric measurement, when projected through the "zero" point on the nomogram, affords a simple, precise means for determining the scleral rigidity coefficient. The normal scleral rigidity coefficient (E) is approximately 0.022, and when this is found significantly altered (e.g., $\pm$ .010 units) the tonographically determined intraocular pressures should be corrected for this factor. When scleral rigidity is lower than normal the intraocular pressure as determined by tonography appears falsely low, as does the coefficient of outflow. The converse is true in the rare cases when scleral rigidity is higher than normal. However, it is quite unlikely that an elevated scleral rigidity would ever lead one to a false diagnosis of glaucoma, especially if one calculated the Po/C ratio and considered the clinical findings.[3]

A *lowered* scleral rigidity, on the other hand, assumes considerable significance in evaluating borderline glaucoma or the status of glaucoma control in myopic patients, individuals who are using miotics, or who have had ophthalmic surgery. The measurements of intraocular pressure in these cases, as determined by tonometry or tonography, will frequently give one a false sense of security. In such cases applanation tonometry, directing one's attention to the falsely low outflow facility, or correcting the intraocular pressure for scleral rigidity will reveal the true situation.

One can compute the actual rate of aqueous secretion from the data furnished by tonography by employing the formula $F = C$ (Po-10). It is usually not practical nor necessary in office practice to do this, since one can estimate the secretory status with sufficient clinical accuracy by comparing the level of intraocular pressure with the adequacy of outflow. If intraocular pressure is low in the presence of a relatively poor outflow facility, the state of "hyposecretion" exists. When intraocular pressure is high in the presence of a relatively good outflow facility, the state of "hypersecretion" exists.

Of course the main criterion of whether "control" is adequate is evaluation for the loss of visual field. Tonographically one attempts to maintain an intraocular pressure of less than 20 (considerably less if possible), and one strives to maintain a coefficient of outflow better than 0.20 (and certainly better than 0.15). The Po/C ratio should be maintained below 100. When these factors show evidence of poor control, intensification of medical therapy or appropriate surgical intervention is indicated.

It is of significance that an abnormally low scleral rigidity coefficient will be reflected by a flat tracing on the tonogram which mimics that found in "hyposecretion glaucoma." Likewise elevated scleral rigidity is characterized by a steep tracing which simulates that found in "hypersecretion glaucoma." Consequently, before one can diagnose these specific varieties of glaucoma one must consider the influence, if any, of the scleral rigidity factor.

Interpretation of the tonogram is best accomplished when one has knowledge of other correlative clinical findings. Some of the

pertinent factors which influence one in the interpretation of the tonogram, and deciding on appropriate management of specific cases will be briefly enumerated. These include: (a) artifacts of the tonographic curve, (b) family history of glaucoma or clinical history suggesting glaucoma, (c) age, (d) effect of mydriasis, (e) effect of water drinking, (f) specific types of glaucoma (e.g., hypersecretion, masked angle of closure, hyposecretion, etc.), (g) gonioscopy, (h) visual fields, (i) ability to return for re-evaluation, (j) ability to cooperate with medical therapy, (k) scleral rigidity factor, (l) pigmentary glaucoma, and (m) secondary glaucoma.

Case Illustrations

Case 1 illustrates an artifact in the tonographic curve in a 40 year old man, the intraocular pressure being estimated by extrapolation of a straight line, corresponding to the general slope of the tonographic pattern (Fig. 2). (An applanation tonometric measurement of the initial and final pressures would have afforded an alternate method of correcting for this devious curve.) The initial intraocular pressure (Po) is 20, the outflow coefficient (C) is 0.18. The Po/C ratio is greater than 100. These findings become even more significant after water drinking (Po 23, C .16). The anterior chamber is wide on gonioscopy. Even though field loss is not demonstrable, this patient probably has glaucoma. However, since he is intelligent, cooperative, and lives in town, miotic therapy is being withheld, and he will return in 3 months for another water provocative test, and field determination.

The latter is considered to be of major clinical significance in managing such cases.

Case 2 is that of a 53 year old man whose history revealed the symptom of intermittent "halos" around lights, especially at night, and in the movies. Gonioscopy revealed the presence of very narrow, potentially occludible angles (the ciliary body band was not visible), but there were no peripheral anterior synechiae. Visual field examination showed "baring of the blind spot." A mydriatic provocative test elevated the Po from 22 to 30, and the C value was simultaneously reduced from 0.20 to 0.15. This case represents "angle closure glaucoma," and is best handled by prophylactic iridectomy (Fig. 3).

Case 3 concerns a 47 year old woman with known glaucoma, proven by loss of fields. She was emotionally unstable and had labile hypertension. Her tonogram reveals a Po of 34 (on miotics), and a C value of 0.26. Her scleral rigidity is essentially normal, being 0.024. She is one of the rare cases of "hypersecretion glaucoma," and one can predict that she will be difficult to control. Surgical treatment should not be used early in such cases, as these patients usually do poorly. Diamox should be added to her regimen, and, if necessary, epinephrine, to reduce the aqueous secretion (Fig. 4).

Case 4 portrays a steep tonographic curve suggesting "hypersecretion glaucoma." History of intermittent episodes of blurred vision at night, and gonioscopic evidence of angle closure at the height of an attack, reveal the proper interpretation of the tonogram to be "masked angle closure." Field loss is present but minimal. Since the outflow coefficient is 0.21, a peripheral iridectomy should be beneficial.

FIG. 2

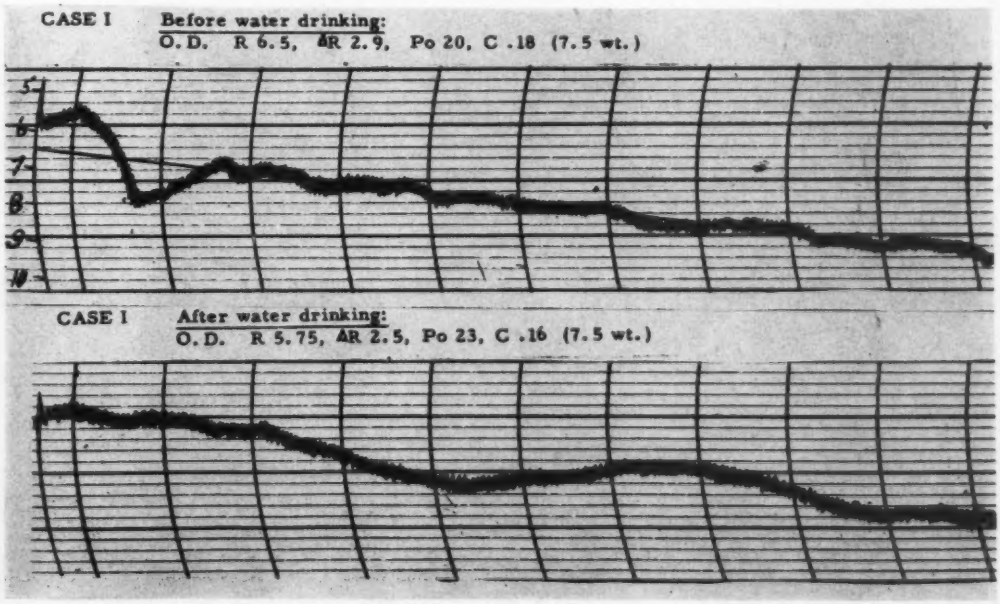
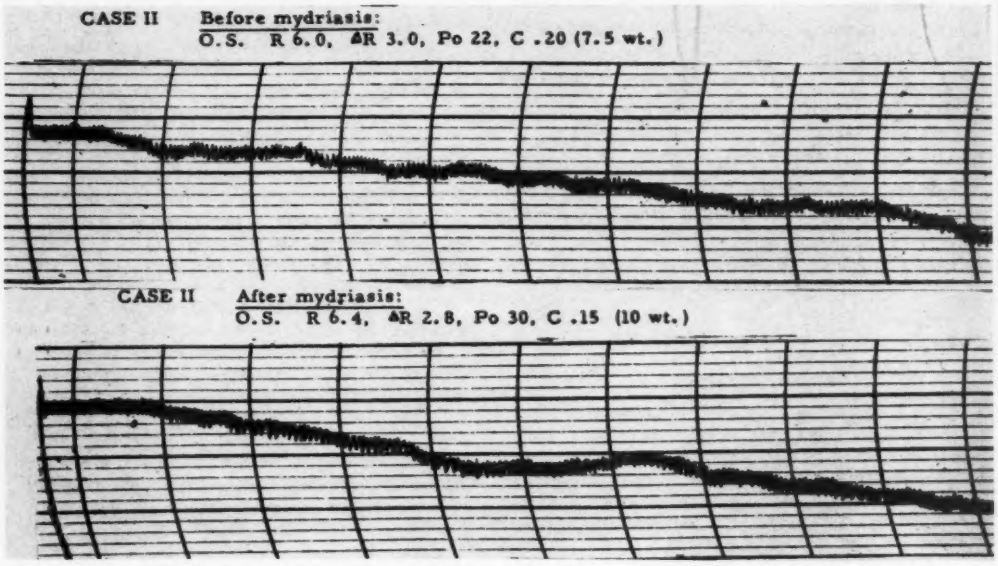


FIG. 3



Case 5 represents a 37 year old, highly myopic man, with wide open anterior chamber angles. His mother and sister are known to have glaucoma, Schiøtz tonometry, performed in the course of a routine examination, revealed an intraocular pressure of 21. When corrected for low scleral rigidity, the intraocular pressure (applanation) was 26. The Po/C ratio on tonography is 125. Visual field determination showed early field loss. This patient should be started on miotic therapy (Fig. 5).

Case 6 is a patient who has had a peripheral iridectomy for angle closure glaucoma. After correcting for low scleral rigidity the tonogram reveals a Po of 17, and an outflow coefficient of 0.14, indicative of "hyposecretion." This patient bears close watching, since hyposecretion is usually merely a transient, compensatory phase, and is apt to progress into uncontrolled glaucoma in the near future. It would probably be wise to employ miotic therapy in this case to improve the outflow facility, even though intra-

FIG. 4

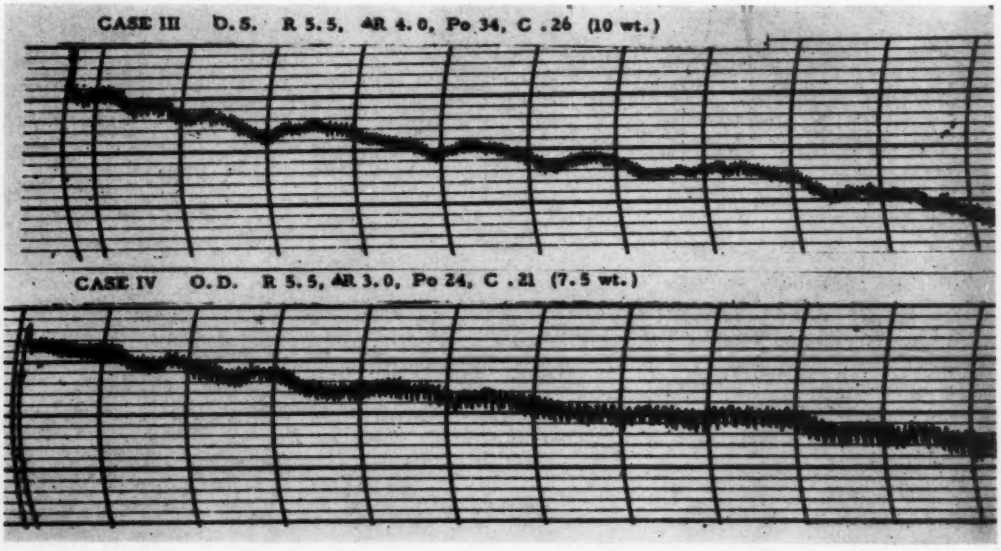
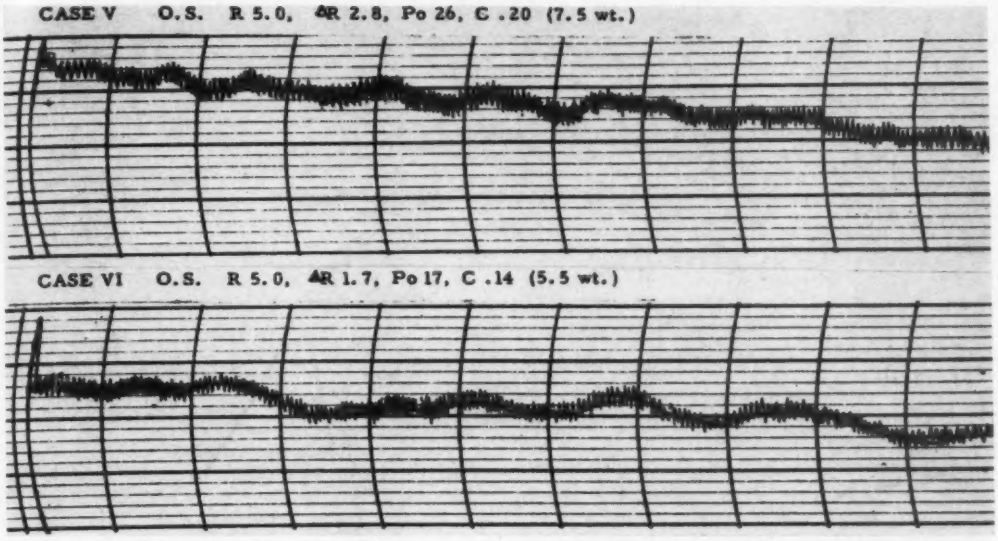


FIG. 5



ocular pressure is still within normal limits.

Case 7 is that of a 41 year old laborer with wide angles, who is intellectually incapable of cooperating in visual field testing, and who is not conscientious in "using his drops." He lives a great distance from any ophthalmologist. His tonogram reveals a Po of 28, and a C of 0.10. It would be well in this instance to perform an iridencleisis or similar procedure (Fig. 6).

Case 8 reveals a Po of 30 and a C value of 0.15. Early loss in visual field is demonstrable. Gonioscopy reveals intense pigmentation of the trabecular meshwork, and on biomicroscopy by slit lamp a Krukenberg spindle is evident. This patient has "pigmentary glaucoma," and should be started on miotics. If necessary, Diamox and epinephrine should be added to the therapeutic regimen. One can predict that this patient's control will be precarious; however, operation should be withheld if control can be otherwise accomplished. These cases are notorious for responding relatively poorly to surgical intervention.

FIG. 6

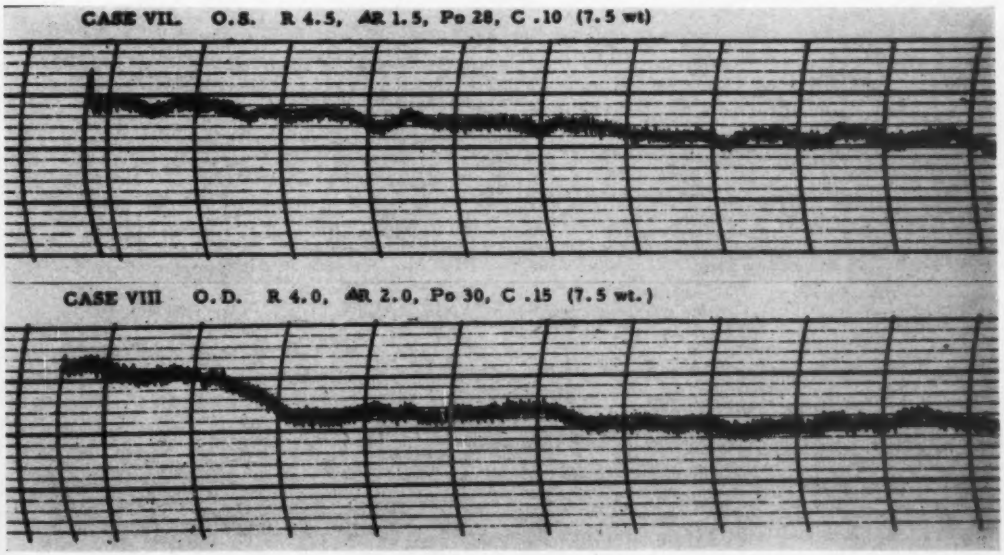
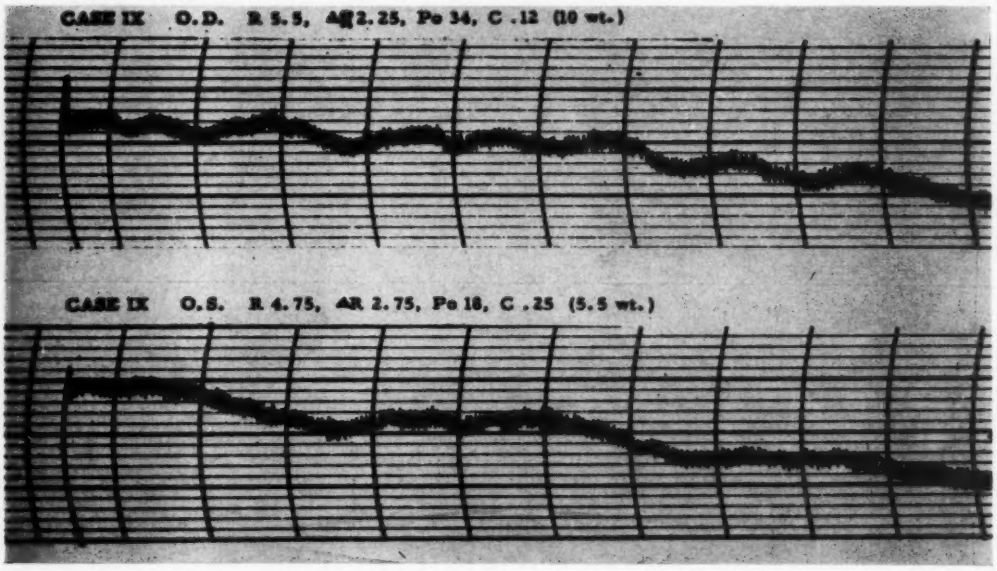


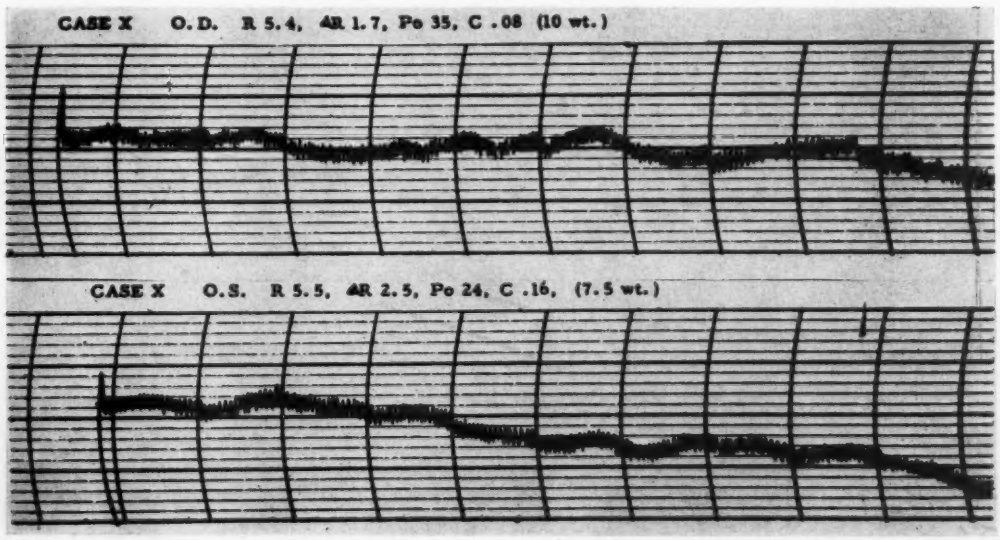
FIG. 7



Case 9 typifies a patient with obvious glaucoma (Po 34, C 0.12) in one eye, whereas the other eye is tonographically normal. This unilaterality should arouse the suspicion of the existence of a "secondary" etiologic factor in the causation of the glaucoma. In this particular case gonioscopy revealed a ciliary body cyst to be embarrassing the anterior chamber angle recess, and surgical removal resulted in a cure of the glaucoma (Fig. 7).

Case 10 is concerned with an individual who has had an occlusion of the central retinal vein in the right eye, in which eye is evident uncontrolled glaucoma (Po 35, C .08). A most significant finding is that in the fellow eye there is indication of primary glaucoma, as shown by the Po/C ratio of 150, which is perhaps even more significant in view of the fact that this is the second eye to undergo tonography. It is well known that the second eye usually records a Po slightly lower than its real value due to obscure reflexes related to tonography of the first eye. This in-

FIG. 8



cidence of bilateral, pre-existing glaucoma characterizes 80% of individuals who exhibit an occlusion of the central retinal vein. A thorough evaluation of the fellow eye in such cases to detect possible glaucoma cannot, therefore, be too highly recommended (Fig. 8).

Summary

Tonography is a valuable adjunct in the clinical diagnosis and management of glaucoma. It is my wish that the case illustrations and foregoing description of clinical tonography may serve to encourage the increased utilization of this worthwhile procedure among ophthalmologists in office practice.

References

1. Clark, W. B.: Symposium on Glaucoma (New Orleans Academy of Ophthalmology, 1957). St. Louis, C. V. Mosby Company, 1959.
2. Schimek, Robert A.: Simplified Tonography (Manual prepared for instruction course at American Academy of Ophthalmology & Otolaryngology, New Orleans) 1959.
3. Becker, Bernard: Personal Communications (Washington University, Department of Ophthalmology, St. Louis), 1959.
4. Moses, Robert A., and Becker, Bernard: Clinical Tonography: The Scleral Rigidity Correction, Am. J. Ophth. 45:196, 1958.

Discussion (Abstract)

Dr. Lyne S. Gamble, Greenville, Miss. Dr. Derivaux has presented a comprehensive summary of the role of tonography in the diagnosis and management of glaucoma. Quite properly he has emphasized the fact that tonography will not reveal the tolerance to elevated intraocular pressure that characterizes any specific optic nerve and the fact that the main criterion of whether or not "control" is adequate is evaluation of visual field loss.

I certainly have nothing to add to this excellent paper, though there are two devices I have found helpful. The first of these is very elementary and is designed to assist those of us who have become very much attached to the tonometric scale of 1948, in the transition to the 1955 scale and the correction for scleral rigidity. This consists of a rubber stamp. Spaces are provided for recording the tonometer readings with any of the desired weights, the tension as it would be read on the 1948 scale, the tension as it would be read on the 1955 scale, the coefficient of scleral rigidity and the corrected tension.

A single pair of tonometric readings may lead to very large errors in the estimation of ocular rigidity and for this reason repeated pairs of tonometric readings (at least six), one pair of readings at each office visit, should be made as suggested by Dr. Kronfeld (Am. J. Ophth. 47:147, 1959). The tonometric readings should be averaged rather than averaging the rigidity measurements.

The second of these devices uses the illustration of Drs. Moses and Becker (Am. J. Ophth. 45:196, 1958) which utilizes the Friedenwald nomogram to portray the changes which take place during tonography. Pressure changes are plotted on the vertical axis. Volume changes are plotted on the horizontal axis. The conditions that exist prior to the application of the tonometer have been represented in blue. The tension in the undisturbed eye (Po) is determined by the applanation tonometer or by paired readings using the Schiøtz mechanical or electronic tonometer. This pair of scale readings defines the oblique line Po-R, the slope of which represents the scleral rigidity, in this case 0.0215. Or if the coefficient of rigidity has been determined previously by the above mentioned method of repeated pairs of tonometric readings, the slope can be established on the quadrant in the lower left-hand corner and the line Po-R constructed parallel to it. As has been mentioned, scleral rigidity may be reduced in myopia, thyrotropic exophthalmos after the water drinking test and after the topical use of anticholinesterase drugs (Humorsol, Phospholine, eserine).

The conditions that exist at the beginning of the tonogram have been represented in green. The tonometer has indented the cornea and displaced fluid of volume V_o. The sclera has been distended and the intraocular tension has been raised to Pt_1 but no fluid has been lost from the eye.

The conditions that exist at the end of the tonogram are represented in red. The cornea has been further indented (V_2), the sclera has partially retracted (V_1) and the intraocular pressure has dropped to Pt_2. The amount of increase in intraocular pressure is termed ΔP. This is determined by adding Pt_1 to Pt_2 and dividing by 2 in order to determine Pt_{av}. Po and ΔP_v (1.25 which is the increase in episcleral venous pressure incident to tonography) are subtracted from Pt_{av}. The amount of aqueous squeezed out by this increased intraocular pressure is termed ΔV and is determined by subtracting V_1 from V_2. t is time and is usually four minutes. These values are then substituted in the equation $C = \frac{\Delta V}{t \Delta P}$ in order to determine the facility of aqueous outflow corrected for scleral rigidity.

In the present state of our knowledge, it appears that most glaucomas are the result of obstruction of the drainage pathway. Tonography provides the most direct method of measuring this obstruction.

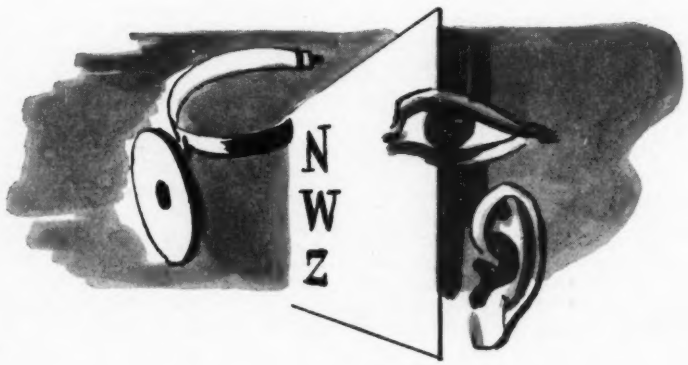
Dr. Robert A. Schimek, New Orleans, La. The title of this paper, "Tonography in Office Practice," indicates a new trend. This is a trend toward more precise detection and management of glaucoma by the typical ophthalmologist in his office for the average patient. No longer are only the research centers solely privileged to use tonography. Tonography is now frequently performed in many private offices in which many cases of glaucoma are seen. This is the natural result of standardization of technic, control of sources of error, improved equipment, and enthusiasm over a new approach.

The versatile applications of tonography include, first, the early detection of wide-angle glaucoma. This may be so early that either the definition of a glaucomatous eye as a damaged eye may need partial revision, or else a term such as preglaucomatous will come into more common usage. Second, the tonographic Po/C ratio will usually permit anticipation of the success or failure of miotic or surgical therapy.

Third, hypersecretion glaucoma can be detected. Conversely, the degree of suppression of aqueous secretion by carbonic anhydrase inhibitors, cyclodiathermy, or cycloelectrolysis can be estimated. Fourth, in angle closure glaucoma, tonography reveals whether normal angle drainage mechanisms can still function efficiently to permit an iridectomy to control the pressure, or if a filtering operation is necessary. Other virtues of tonography could be extolled if time permitted.

On the other hand, there are reasons for the average ophthalmologist to consider carefully before incorporating tonography into his office routine. First, it is not absolutely essential to the management of the usual case of glaucoma, although it is extremely helpful. Also, worthwhile tonography requires some training and investment in equipment. It is time-consuming and demands careful control of potential sources of error. Without adequate technic and interpretation, it would be better to refer patients to a well-equipped center for an accurate tonographic report. However, with precise technic, careful interpretation, and with a sufficient number of consultations on glaucoma, tonography does prove of great value as an office procedure.

I would like to clarify one point that Dr. Derivaux made, in case there was any misunderstanding. The 50% inhibition of aqueous secretion by Diamox is not increased an *additional* 30% by adding epinephrine, but a somewhat smaller amount (to a total of 66% inhibition) as published by Becker.



CASE REPORT

Clostridial Gas Gangrene and Septicemia Complicating Leukemia

LEWIS E. JONES, M.D., WOLFGANG A. WIRTH, M.D., and CYRUS C. FARROW, M.D.,† *Kecoughtan, Va.*

IN A RECENT ARTICLE Boggs, Frei and Thomas,[1] discussed the case histories of 4 patients who developed clostridial gas gangrene and septicemia as a complication of leukemia. This paper presents a similar case and introduces additional features of interest. Briefly, it concerns a patient with a primary diagnosis of chronic granulocytic leukemia complicated by adenocarcinoma of the ascending colon and subsequent clostridial gas gangrene and septicemia which promptly led to death. To our knowledge, this is the first case in which *Clostridium sporogenes* (Metchnikoff) was cultured from the blood both antemortem and postmortem. Therapy with adrenocorticosteroids and antimetabolites was used as in the cases reported by Boggs and associates, and again the possible role of this treatment in precipitating the final complicating episode is considered.

Case Report

A 65 year old white man was first admitted to the Veterans Administration Hospital, Kecoughtan, on April 19, 1956, where he remained until July 30, 1956. A diagnosis of chronic granulocytic leukemia had been made during hospitalization at another hospital in January 1956. During the January hospitalization, the use of prednisolone resulted in improved clinical and laboratory findings. In April 1956, he was admitted to the Veterans Administration Hospital because of recurrent anemia.

In addition to whole blood transfusions, he received 6-mercaptopurine and prednisolone. The dose of 6-mercaptopurine was frequently changed and eventually discontinued on May 21, 1957, because of a pronounced leukopenia and skin rash. Subsequently he improved sufficiently to permit frequent periods of time at home. The final admission, on July 8, 1957, was prompted by a recurrence of anemia and weakness. Very small doses of intramuscular vitamin B_{12} (2.5 mcg. daily) and folic acid (2.5 mg. b.i.d.) separately and together, failed to produce significant changes. These drugs were tried in view of the megaloblastoid erythropoiesis, though extremely small doses of these drugs were employed to avoid the possibility of precipitating a sudden increase in the myeloid elements. During a period from August 12 to October 1, when a number of teeth were extracted, he was given oral penicillin prophylactically. He tolerated the dental treatment very well.

The administration of prednisolone (10 mg. q.i.d.) for 7 weeks, beginning on March 6, failed to provide benefit. The possibility of secondary hypersplenism became apparent, and discussion on several occasions centered around indications for and against splenectomy. After considerable discussion, splenectomy was agreed upon and was performed on May 27, 1958. Except for more than the usual amount of bleeding during and immediately following operation, the postoperative course was smooth. Gross and microscopic examination of the spleen showed changes compatible with hypersplenism; however, no evidence of leukemic infiltration was present.

On the first postoperative day an improvement in the thrombocytopenia and leukopenia was noted, though the differential count of the white blood cells was unchanged. From the 5th to the 10th postoperative days, the platelet count had increased from a low of 80,000 to 300,000 and the WBC. had risen from 3,000 to 9,000. The improved platelet count and a normal leukocyte count persisted for approximately one month. Then the thrombocytopenia worsened again and the total leukocyte count gradually rose to 35,000. The use of 6-mercaptopurine in varying doses and the administration of blood maintained the total blood picture in a relatively satisfactory state. Because of a total leukocyte count of 2,650 on Sept. 22, 1958, 6-mercaptopurine was discontinued. The leukopenia and thrombocytopenia persisted until death.

Beginning in August 1958, fever and night sweats, with a temperature ranging from 100° to 140° (F), occurred on several evenings. These episodes were considered as effects of the leukemic process. On September 8, the left forearm was swollen, warm, and slightly tender. The use of penicillin resulted in local improvement, but fever and night sweats continued. After obtaining bacteriologic specimens, including

†From the Medical Service, and with the technical assistance of Mr. Clarence Gaskins, Medical Illustration Service, Veterans Administration Hospital, Kecoughtan, Va. Drs. Wirth and Farrow are Residents in the Department of Pathology, the DePaul Hospital, Norfolk, Va.

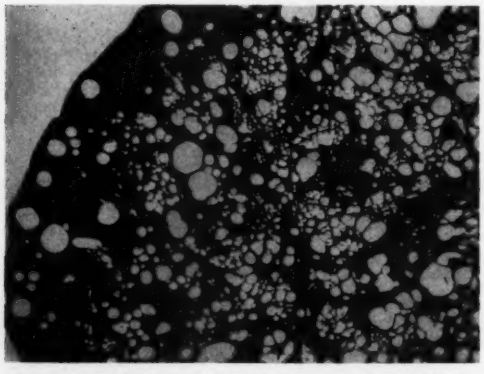
several blood specimens for culture, he again received penicillin (4 million units every 6 hrs.) but no improvement resulted. Therapy was changed to a combination of erythromycin (500 mg. every 6 hrs.) and chloramphenicol (500 mg. every 6 hrs.), and within 36 to 48 hours the fever began to subside and soon returned to normal. Bacteriologic studies were negative.

Despite frequent administration of blood during October and November 1958, the anemia recurred more rapidly, and for this reason blood loss was suspected. Stool guaiac studies were strongly positive. Additional treatment consisted of an ulcer diet and antacids.

On the evening of November 23, five days following cessation of antibiotic therapy, the patient had a sudden elevation of temperature to 103° accompanied by a chill. The next morning he became extremely weak and collapsed while in the bathroom but did not lose consciousness. Blood pressure was 100/60, the pulse was not rapid, and there was no sweating. He was placed in an oxygen tent and whole blood was given. After obtaining a blood specimen for culture, treatment with chloramphenicol was initiated. Within a matter of 4 to 6 hours the patient became completely unresponsive. This very rapid downhill course continued and he died approximately 6½ hours after the onset of this last episode of fever. About 3 hours following completion of the autopsy, the mortician reported that marked swelling of the body occurred following its arrival at the funeral home. The blood specimen obtained before death was positive for *Clostridium sporogenes* and microaerophilic streptococcus. Examination of the bacteriologic specimens obtained at the time of autopsy duplicated this finding.

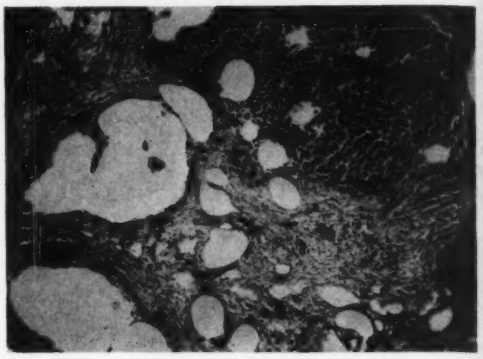
Autopsy Findings. The body was that of a husky, well-developed white man. The skin of the neck, chest, abdomen and extremities was tense, puffy and crepitant. This was striking, especially within the skin of the scrotum which was distended, measuring 10 by 10 cm. at its widest point. The lungs were voluminous and wet. The spleen was absent. The liver, weighing 2,600 Gm., filled the entire epigastrium. The capsular surface was finely nodular and the organ was firmer than usual. The cut surface revealed foamy areas and visible small gas bubbles giving it a finely honey-combed appearance. The gastric mucosa was lined with air blisters, which occasionally were confluent. The small intestine was distended by gas. In the ascending colon, 15 cm. from the ileocecal valve, an ulceration 2 cm. in diameter was found which had a mushy, granular bed and circumferential induration. The wall of the colon about the ulcer was thickened and edematous. Six polyps were found in the colon. The only other significant gross finding was soft greyish-tan bone marrow of the iliac crest, vertebral column and sternum.

FIG. 1



Cut surface of liver (8 x). Note the innumerable gas bubbles.

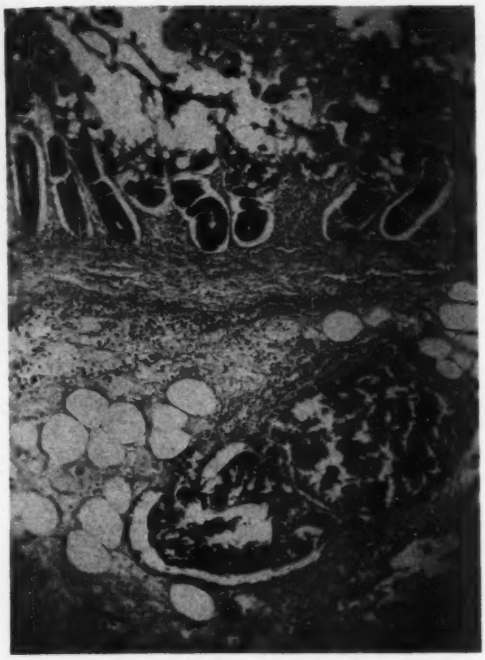
FIG. 2



Cut surface of liver (75 x). Note the distortion of the lobular pattern by the increased connective tissue and gas bubbles.

Microscopic examination of the liver showed a lace-like pattern due to distortion by gas bubbles (Fig. 1). The lobular pattern was altered by a marked increase in interstitial connective tissue which surrounded pseudolobules containing peripherally displaced central veins (Fig. 2). Autolysis and/or necrosis obscured hepatic cellular details. Frequent clusters of gram positive rods of a safety-pin appearence were seen. A section from the ascending colon was lined by smudgy, eosinophilic columnar cells in which no details were recognizable. In some areas the epithelial lining was missing and the surface was covered by a homogeneously eosinophilic material. The mucularis mucosa occasionally was interrupted by nests of smudgy, eosinophilic cuboidal to columnar epithelial cells, arranged in a glandular fashion. The lumen of these neoplastic glands contained strands of a mucicarmine-positive material. Within the submucosa similar, but larger, structures were present (Fig. 3). In this area cellular details were somewhat preserved. The epithelial cells had large nuclei with two or more nucleoli. At the periphery of the large glandular structures the epithelial cells were arranged in a cribriform pattern. The mucosa and submucosa were markedly thickened. A diffuse cellular infiltrate was present consisting mainly of histiocytic mononuclear cells and scattered neutrophils. The muscularis proper and the thickened and edematous subserosa contained spotty lymphocytic infiltrates. A large number of gram positive rods were seen singly and in clusters

FIG. 3



Ascending colon (75 x). Note the diffuse edema, inflammatory infiltration and the nests of neoplastic glands within the submucosa.

within the mucosa and submucosa, especially adjacent to the neoplastic glands. The bone showed osteoporosis and fibrosis of the marrow. An increased number of immature cells of the granulocytic series was seen and a few eosinophils also were present. The number of red blood cells appeared to be sufficient. Frequently, large air bubbles were present within the bone marrow in association with numerous gram positive rods.

Discussion

A comparison of this case report with those previously reported by Boggs, Frei and Thomas[1] revealed several common features and two significant differences. The primary diagnosis in all patients was leukemia (3 granulocytic, 1 lymphocytic and 1 monocytic). All patients had received adrenocorticosteroid and antimetabolite drugs as treatment (4-amino-N-methyl pteroylglutamic acid [Methotrexate], 6-mercaptopurine or triethylene melamine). The onset of the complication due to clostridium was abrupt with rapid acceleration of the illness in all cases. Bleeding from the lower intestinal tract occurred in 4 of the 5 cases during the acute terminal phase of the disease. In all cases, autopsy examination revealed excess gas in the body cavities and subcutaneous tissues, and also crepitation of various organs. The portal of entry in all cases probably was in the intestinal tract; however, the intestinal lesion in our case was a small adenocarcinoma of the ascending colon rather than leukemic infiltration. Intravascular hemolysis was noted in all of the cases reported by Boggs and associates but was absent in this case. This feature is not surprising since only in exceptional cases does *Clostridium sporogenes* produce a hemolytic toxin;[2] however, it does form a strong proteolytic enzyme which may explain the rapid decomposition in this case.

A variety of anaerobic bacilli normally inhabit the intestinal tract. In one study *Cl. welchii A* & *B* were found in 46 of 55 normal appendices.[3] That anaerobic bacilli are well tolerated under normal circumstances has been further substantiated by volunteers who ingested *Cl. perfringens* without suffering ill effects. It has been emphasized that intestinal secretions, and especially bile, inhibit the growth of *Clostridia*.[2]

Alteration of physiologic conditions might permit the anaerobic bacilli to become pathogenic. Experimental obstruction of the gastrointestinal tract has resulted in fatal peritonitis in which the peritoneal exudate contained the highly toxic lecithinase of *Cl. perfringens*. These experiments show that anaerobic organisms, to act as pathogens, need damaged tissue with decreased oxygen tension.[2] Strangulated hernias, perforated appendices, tuberculous and uremic ulcers of the intestine, and carcinoma of the colon have all provided portals of entry for *Cl. perfringens*. Intrauterine trauma, especially during pregnancy, is a well known cause of septicemia, due to gas forming organisms.[2,4] Less commonly, the gallbladder has been incriminated as a source and in a few cases chemical burns of the gastric wall resulted in fatal clostridial invasion. Relatively minor operations such as tonsillectomies and tooth extractions have been followed by fatal infections. Transurethral* resections of the prostate gland have provided a portal of entry. For a complete discussion of sources of anaerobic infections the reader is referred to the Monograph of Zeissler, Krauspe, and Rassfeld-Sternberg.[2]

All of these conditions have one common

denominator, namely, a localized destruction of tissue which provides a suitable medium for growth and entry. The lesions mentioned above, however, are not rarities and it seems remarkable that clostridial infections do not occur more frequently. Tumors of the intestinal tract rarely lead to gas gangrene at the site of the lesion, even though it appears that necrotic tissue would provide an ideal medium. Therefore, other factors must be necessary to promote bacterial growth and spread.

Certainly the humoral and cellular defenses of the blood and tissues play a most important role in combating infectious processes. The cases published by Boggs, Frei and Thomas and this case had bone marrow depression following treatment with cytostatic drugs. How much added insult this chemotherapy contributed is a matter of conjecture. One might theorize that if necrosis resulted, multiplication and growth of bacteria might have been benefited. It is possible that the neutropenia was an expression of an alteration in cellular defense and thereby provided a more suitable environment for the spread of clostridial organisms from the intestinal site.[5] The impaired cellular defense mechanism in leukemia is known. In the case presented, treatment with 6-mercaptopurine resulted in long-standing bone marrow depression. It might be speculated that the humoral defense had been impaired by the administration of cytostatic drugs through a decrease in the number of plasma cells, thereby reducing the amount and rate of antibody formation.[6] The autopsy findings do not permit a definite statement in this regard, since a small number of plasma cells were present in the lymph nodes and bone marrow. It appears that the carcinoma offered a satisfactory medium for entry, growth and spread of the organisms and that the impaired humoral and cellular defenses permitted the rapid development of the septicemia.

It is probable that the changes in the liver might have resulted from treatment with 6-mercaptopurine and steroids since recently the development of toxic hepatitis has been reported in four patients who were being treated for leukemia with 6-mercaptopurine and steroids.[7]

Summary

1. A case report is presented of a patient who developed gas gangrene and septicemia due to *Clostridium sporogenes*, complicating chronic granulocytic leukemia. No evidence of leukemic infiltration was found within the intestinal tract. This is the first reported case in which this complication has been due to the sporogenes strain, which is usually nonpathogenic. This report brings the total to 8 cases related to neoplastic disease, 5 of which were related to leukemia.

2. The portal of entry of the gas forming organisms was an unsuspected small adenocarcinoma of the ascending colon, and thereby in this case differed from previously reported cases of leukemia in which leukemic infiltration of the bowel served as the portal of entry.

3. The absence of intravascular hemolysis was an additional distinguishing feature in this case. This variation occurred since *Cl. sporogenes* do not form a hemolytic toxin.

4. The possible role of cytostatic drugs in increasing the susceptibility to clostridial infection is discussed. The clinician should be aware of the increased potential danger of bacterial spread associated with the use of cytostatic drugs and be prepared to act quickly if infection develops.

References

1. Boggs, D. R., Frei, E., III, and Thomas, L. B.: Clostridial Gas Gangrene and Septicemia in Four Patients with Leukemia, New England J. Med. 259:1255, 1958.
2. Zeissler, J., Krauspe, C., and Rassfeld-Sternberg, L.: Die gasoedeme des menschen, Vol. 1, 1958, Dr. Dietrich Steinkopf Verlag, Darmstadt, p. 154.
3. Loehr, W., and Rassfeld, L.: Die bacteriologie der wurmfortsatzentzuendung und der appendikularen peritonitis, Georg Thieme Verlag, Leipzig, 1931, p. 37.
4. Mahn, H. E., and Dantuono, L. M.: Postabortal Septicotoxemia due to Clostridium Welchii: Seventy-five Cases from Maternity Hospital, Santiago, Chile, 1948-1952, Am. J. Obst. & Gynec. 70:604, 1955.
5. Moore, G. E., and Watson, T. G.: Triethylenethiophosphoramide Therapy Complicated by Overwhelming Infection with Clostridium Welchii: Report of Two Cases, Cancer 10:246, 1957.
6. Kelsall, M. A., and Crabb, E. D.: Lymphocytes and Plasmocytes in Nucleoprotein Metabolism, Ann. New York Acad. Sc. 72:293, 1958.
7. McIlvanei, S. K., and McCarthy, J. D.: Hepatitis in Association with Prolonged 6-Mercaptopurine Therapy, Blood 14:80, 1959.

CASE REPORT

Rocky Mountain Spotted Fever with Thrombocytopenia

CAREY W. PHILLIPS, JR., M.D., *Birmingham, Ala.*,
GEORGE T. KIMBROUGH, M.D., *Jackson, Miss.*,
JEROME A. WEAVER, M.D., and ALEX L. TUCKER, M.D.,
Birmingham, Ala.

THREE PATIENTS WITH ROCKY MOUNTAIN spotted fever were admitted to Children's Hospital, Birmingham, during July 1958. Thrombocytopenia complicated the clinical course of one patient with resultant delay in definite diagnosis. Although thrombocytopenia has been observed in other rickettsial disease, it has not been reported in Rocky Mountain spotted fever.[1]

Rocky Mountain spotted fever was described by physicians and scientists of American medicine who also established the etiology[2] and developed specific therapy.[3] This serious disease in children has been reported in 46 states of the United States; cases have not been reported for Maine, Vermont, Alaska, or Hawaii. In the last two states, there is no vector of the disease.[4,8] The dog tick *(Dermacentor variabilis)* is the vector in the eastern United States, and children are primarily affected because of their comradeship with dogs.

Rocky Mountain spotted fever, which is most prevalent in the eastern United States during June, July, and August,[5] has an incubation period varying from 2 to 14 days. (The average is 6 to 7 days.)[6] A history of tick bite is helpful in making a diagnosis, although at times it cannot be obtained. The early symptoms consist of malaise, anorexia, headache, photophobia, followed by sudden onset of fever and chills, perhaps prostration, marked myalgia, and arthralgia. As the disease progresses, disorientation and generalized muscle tenderness become pronounced, often obscuring other symptoms. The most important diagnostic sign is the rash, which usually appears on the third or fourth day of the disease; in a few instances, the rash is seen during the first 24 hours. The discrete red, macular rash, which blanches on pressure, initially resembles rubeola. Within hours it becomes papular with subsequent formation of well-demarcated petechiae. The rash usually is found first on the ankles and flexor surfaces of the wrists, and spreads proximally to involve the trunk. This differs from measles which begins on the face and typhus which begins on the trunk. In severe cases the entire body is covered by the rash, including the palms, soles, and oral mucosa. (In typhus the palms, soles, and oral mucosa are not involved.) The temperature has peaks as high as 105°F. with irregular morning remissions. This usually occurs during the second week of the illness. Once the disease responds to broad spectrum antibiotics, there is rapid lysis of fever barring secondary infections.

The differential diagnosis must include diseases characterized by fever and petechiae. Among these are: (1) other rickettsial diseases; (2) septicemia (especially meningococcal); (3) rubeola; (4) blood dyscrasias; (5) infectious mononucleosis; (6) drug reactions; and (7) anaphylactoid purpura.

Following earlier symptomatic treatment, sulfonamides were used as specific treatment but later were found to be contraindicated.[7] The first effective drug discovered was para-aminobenzoic acid, a sulfonamide antagonist.[9] The broad spectrum antibiotics are now the treatment of choice.[3]

The etiologic diagnosis[6] of Rocky Moun-

tain spotted fever is made by the Weil-Felix reaction and the more specific complement fixation test. All three types of *Proteus vulgaris* (OX-19, OX-2, OX-K) may be agglutinated by the patient's serum; however, the highest titer typically occurs with the OX-19 strain. It should be emphasized that the Weil-Felix reaction identifies the rickettsial group, but does not differentiate the specific rickettsial diseases. The complement-fixation test does differentiate the various rickettsial diseases. Complement fixing antibodies usually appear during the second or third week of the disease in untreated patients, but may be delayed one to two weeks in patients treated early. As in all serologic tests, the serum specimens must be paired, since only a rise in specific antibody titer of four-fold or more is positive evidence of current infection with the responsible agent.

Case Report

Present Illness: A 6 year old white boy (Children's Hospital—A 18221) was admitted with a 7 day history of anorexia, malaise, headache, and fever. Four days prior to admission, he developed a macular rash over the arms and legs which spread to involve the trunk, face, and neck. Myalgia and arthralgia then became prominent features of his illness. He was treated by his family physician with penicillin, sulfadiazine and aspirin without response or abatement of the fever. He was then referred for further evaluation.

The patient consumed well water, raw milk, and used an outdoor toilet. Two siblings were living and well. Dogs and cats were family pets, but contact with birds and rabbits was denied. Ticks were removed from dogs at their home in the past few weeks. No definite history of tick bite was obtained. Immunizations had been completed only against diphtheria, tetanus and pertussis.

Physical Examination: The skin was dry and hot with a petechial rash generalized over the extremities, thorax, face, and neck. There was mild injection of the conjunctivas and pharynx. There was slight nuchal rigidity. The lungs were clear to percussion and auscultation. The examination of the heart revealed tachycardia without murmur or thrills. The abdomen was soft, with a palpable liver and a spleen 2 cm. below the costal margin; no other masses were palpable. The extremities were tender to palpation, especially at the joints, but no inflammation or edema of the joints was found. Neurologic examination was negative.

Hospital Course: The initial impression was meningococcemia. Spinal fluid, blood, nose, throat cultures, and agglutinations were obtained. The cerebrospinal fluid contained 2 lymphocytes, protein 13 mg. and glucose 54 mg. per 100 cc., and chlorides of 118 mEq./L. Treatment was then begun with sulfadiazine and chloramphenicol.

A positive tourniquet test was present on the day after admission, at which time the bleeding time was 2 minutes, clotting time 4¾ minutes, and the platelet count 21,550. Proteus OX-19 was positive 1:40 on July 25, 1958. The other agglutination and the heterophile antibody tests were negative. Megakaryocytes were sharply diminished in sternal bone marrow, with platelets almost absent. A marked leukemoid reaction was noted with toxic granulations in the white blood cells. The sulfadiazine was discontinued 24 hours after admission and chloramphenicol 250 mg. every 6 hours was begun. The platelet count continued to rise, and on July 26, was 99,750. The patient remained very ill with delirious and lucid intervals. Clinically he appeared worse with hyperpyrexia, marked myalgia and arthralgia. By the 4th hospital day, definite improvement was noted. At this time, the proteus OX-19 titer was positive 1:320 and the complement fixation for *Rickettsia rickettsii* was positive 1:64. Two days later the OX-19 titer was 1:640, with a rise in the platelet count to 303,630 The myalgia and arthralgia disappeared, and the rash gradually subsided. The patient continued to respond to chloramphenicol therapy and was discharged on the 12th hospital day.

The possibility of the thrombocytopenia being due to sulfonamides or aspirin was considered. This was ruled out by doing complete blood counts and platelet counts prior to, and after one week of sulfadiazine in therapeutic dosage. The same procedures were performed using aspirin.

The platelet count prior to this trial was 268,720; after receiving 45 gr. of sulfadiazine daily for one week, it was 307,300. The following week 20 gr. of aspirin was given daily; the platelet count at the end of one week was 256,870.

Summary

A case of Rocky Mountain spotted fever with an unusual finding of associated thrombocytopenia is reported.

1. The clinical findings and laboratory features of most value for the diagnosis of Rocky Mountain spotted fever are presented.

2. Other febrile illnesses with associated hemorrhagic rashes are considered on differential diagnosis.

3. The specific treatment of Rocky Mountain spotted fever with broad-spectrum antibiotics is recommended.

1947 Warrior Road

References

1. Wintrobe, W. M.: Clinical Hematology. Philadelphia, Lea & Febiger, 1956.
2. Ricketts, H. T.: Contributions to Med. Science, University of Chicago Press, 1911.
3. Pincoffs, M. D., Guy, E. G., Lister, L. M., Woodward, T. E., and Genadal, J. E.: The Treatment of Rocky Mountain Spotted Fever with Chloromycetin, Ann. Int. Med. 29:656, 1948.
4. Gibson, Harry V.: Personal Communication, Commissioner of Health, Alaska Dept. of Health.

5. Harrell, G. T.: Rocky Mountain Spotted Fever, Medicine 28:333, 1949.
6. Laboratory Diagnostic Procedures for Viral and Rickettsial Diseases, U. S. Dept. Health, Education and Welfare, June, 1956.
7. Rivers, T. M.: Viral and Rickettsial Infections of Man. Philadelphia, J. B. Lippincott Company, 2nd Edition, 1952.
8. Enright, James R.: Personal Communication, Hawaii Dept. of Health, Chief Bureau of Epidemiology.
9. Yeomans, A., Snyder, J. C., Murray, E. S., Zarafonetis, C. J. D., Ecke, R. S.: The Therapeutic Effect of PABA in Louse Borne Typhus Fever, J.A.M.A. 126:349, 1944.

ST. LOUIS

FOR

NEXT MEETING

OCT. 31 — NOV. 3, 1960

MAKE PLANS NOW TO ATTEND!

Sexual Behavior of Manic Patients:

A Preliminary Report*

J. B. ALLISON, M.D., and W. P. WILSON, M.D.,† *Galveston, Tex.*

It has commonly been accepted that the manic patient is erotic and sexually aggressive. This study of a small series of patients, equally distributed between the sexes, reveals an increased libido and sexual provocativeness in a higher percentage of women than men.

IT IS THE GENERAL CONCENSUS among psychiatrists that sexual desire and enterprise are usually increased in the manic phase of a manic-depressive illness. Many references to this may be found in the literature. Examples are: Campbell,[1] ". . . A hypomanic or manic is sexually aggressive and often promiscuous in his sexual habits." Bellack,[2] "In the manic . . . there may be alcoholic and sexual excesses which are passed off with the best of cheer." Noyes and Kolb,[3] "The hypomanic is often erotic and may indulge in sexual excesses . . . and may become sexually promiscuous." Davidson,[4] "Sexual freedom is sought in both phases of the manic-depressive."

Kinsey and associates[5] report that "in spite of widespread and oft repeated emphasis on the supposed differences between female and male sexuality, we fail to find any anatomic or physiologic basis for such differences." This leads one to think that most, if not all, of ones sexual desire and enterprise is determined by psychologic factors. However, it was the extreme variability of display of increased sexual desire, as well as the often paradoxical lack of increase and, at times, actual decrease in sexual enterprise, that led us in an attempt to determine what factors in the patient's personality might influence the development of symptoms referable to the sexual sphere.

Patient Material and Methods

Twenty-four manic-depressive manic patients, 12 male and 12 female, are included in this preliminary report. They were obtained from patients admitted to the Neuropsychiatric Division of The University of Texas Medical Branch Hospitals at Galveston, between January and August, 1959. Of the patients included, none had any evidence of basic schizophrenic symptomatology in their illness. Evaluation of the patient's display of sexuality was based on observation of the patient by the physician in charge, the nurses and the patient's relatives. Historical data was obtained from the patients and the patient's relatives. The sexual history included a determination of heterosexual, orogenital and auto-erotic activities during the illness and in the pre-illness state. Correlations were made between manifest sexuality and age, sex, religion, occupation, type of reaction, duration of illness, previous attacks, marital status, premarital experience, marital sexual adjustment and libido.

Sexual display during illness was graded from 0 to 4+, with 0 indicating no mention of sex, 1+ indicating occasional mention of sex but not flirtation, 2+ indicating frequent mention of sex and some flirtation, 3+ indicating constant talk of sex and flirtation, and 4+ being openly seductive with sexual overtures, physical or verbal.

Likewise, frequency of sexual relations, with the exception of premarital and masturbatory data, was graded from 0 to 4+, with 0 indicating infrequent relations, 1+ indicating one time every two weeks to one time per week, 2+ indicating 2 to 3 times per week, 3+ indicating 4 to 6 times per week and 4+ indicating daily or more.

Premarital and masturbatory data was graded as none, rare, occasional and frequent.

Results

Of the 24 patients studied, 12 were male and 12 were female. At the time of the study,

*Read before the Section on Neurology and Psychiatry, Southern Medical Association, Fifty-Third Annual Meeting, Atlanta, Ga., November 16-19, 1959.

†From the Department of Psychiatry, The University of Texas Medical Branch, Galveston, Tex.

16 were married, 4 had never been married, 3 were divorced or separated and one was a widow (Table 1). Ages varied from 20 years to 67 years with the majority being between 30 to 50 years of age (Table 2). Seven were Catholic, 17 were Protestant and none were Jewish (Table 3). The type of reaction was distributed as follows: 11 were classified as hypomanic, 7 as mania, 5 as acute mania and one as delirious mania (Table 4). Thirteen had been ill for less than one month, 4 for one to two months and 4 for more than three months (Table 5). Of the patients studied, 9 were having their first episode, 9 had had one to three previous episodes and 6 had had more than three previous episodes (Table 6). Patients' social class was determined by Hollingshead's two-factor index[6] and none were Class I, 6 were Class II, 11 were Class III, 6 were Class IV, and one was Class V (Table 7).

From the data available there seemed to be no relationship between the patient's age, religion, duration of the illness, previous episodes or social class and their display of sexuality during their illness. The important factors seemed to be the patient's sex, marital status, marital-sexual adjustment and premarital experience.

TABLE 1

MARITAL STATUS

	Male	*Female*	*Total*
Married	11	5	16
Single	0	4	4
Divorced or separated	1	2	3
Widowed	0	1	1

TABLE 2

AGE

	Male	*Female*	*Total*
20-29	1	3	4
30-39	4	5	9
40-49	3	2	5
50-59	4	1	5
60-69	0	1	1

TABLE 3

RELIGION

	Male	*Female*	*Total*
Catholic	4	3	7
Jewish	0	0	0
Protestant	8	9	17
Baptist	2	4	6
Methodist	2	3	5
Presbyterian	2	0	2
Church of Christ	1	1	2
Lutheran	0	1	1
Unitarian	1	0	1

TABLE 4

TYPE

	Male	*Female*	*Total*
Hypo	3	8	11
Mania	3	4	7
Acute	5	0	5
Delirious	1	0	1

TABLE 5

DURATION

	Male	*Female*	*Total*
0-1 month	7	6	13
1-2 months	3	3	6
2-3 months	0	1	1
More than 3 months	2	2	4

TABLE 6

PREVIOUS EPISODES

	Male	*Female*	*Total*
None	4	5	9
1	2	2	4
2	2	2	4
3	0	1	1
More than 3	4	2	6

TABLE 7

SOCIAL CLASS

	Male	*Female*	*Total*
Class I	0	0	0
Class II	3	3	6
Class III	6	5	11
Class IV	3	3	6
Class V	0	1	1

An important finding was the difference in the degree of sexual display and/or provocativeness by sex. Of the 12 men, 6 were classified as 0, 3 as 1+ and 3 as 2+. The 12 women were broken down as follows: 2 as 0, 3 as 1+, 6 as 2+, none as 3+ and 7 as 4+ (Table 8). It is clear that the women were far more active in their display of sexuality and seductiveness than the men.

TABLE 8

SEXUAL DISPLAY OF PROVOCATIVENESS

	Male	*Female*	*Total*
0	6	2	8
1+	3	0	3
2+	3	3	6
3+	0	0	0
4+	0	7	7

None of the men were classified as 3+ or 4+, whereas 2 out of the 3 Catholic women and 5 out of the 9 Protestant women were classified as 4+ (Table 9).

Two of the 5 married women, 2 of the 4 single women and 3 of the 3 divorced, separated or widowed women were classified as 4+. As mentioned before, none of the men were classified as 4+ (Table 10).

Of the 7 single, widowed, divorced or separated women, both of the 2 with no pre-illness heterosexual activity were classified as 4+, 2 of the 3 with occasional heterosexual activity were classified as 4+ and one of the two with frequent heterosexual activity were classified as 4+ (Table 11).

Another finding that differed in the male and female groups was the level of pre-illness sexual activity as compared with their sexual display during their illness. Eighteen per cent (2/11) of the married men showed an increase in their sexual display or talk during illness, whereas 40% (2/5) of the married women had an increase (Tables 12 and 13).

TABLE 9

SEXUAL DISPLAY VS. RELIGION

	Catholic		*Protestant*	
	Male	*Female*	*Male*	*Female*
0	2	0	4	2
1+	2	0	1	0
2+	0	1	3	2
3+	0	0	0	0
4+	0	2	0	5

TABLE 10

MARITAL STATUS VS. SEXUAL DISPLAY

	Married		*Single*		*Divorced, Separated or Widowed*	
	Male	*Female*	*Male*	*Female*	*Male*	*Female*
0	6	1	0	1	0	0
1+	3	0	0	0	0	0
2+	2	2	0	1	1	0
3+	0	0	0	0	0	0
4+	0	2	0	2	0	3

TABLE 11

PREMARITAL ADJUSTMENT VS. SEXUAL DISPLAY

	Single, Separated, Divorced or Widowed Females		
	Pre-illness Heterosexual Adjustment		
	None	*Occasionally*	*Frequently*
0	0	1	0
1+	0	0	0
2+	0	0	1
3+	0	0	0
4+	2	2	1

TABLE 12

MARITAL ADJUSTMENT VS. SEXUAL DISPLAY
MALE

Sexual Display	*Pre-illness Marital Adjustment*				
	0	1+	2+	3+	4+
0	0	0	3	2	0
1+	1	1	4	0	0
2+	0	0	0	0	0
3+	0	0	0	0	0
4+	0	0	0	0	0

TABLE 13

MARITAL ADJUSTMENT VS. SEXUAL DISPLAY
FEMALE

Sexual Display	*Pre-illness Marital Adjustment*				
	0	1+	2+	3+	4+
0	1	0	0	0	0
1+	0	0	0	0	0
2+	0	0	2	0	0
3+	0	0	0	0	0
4+	0	0	2	0	0

TABLE 14

MASTURBATORY ACTIVITY

	Male	*Female*	*Total*
Pre-illness			
None to rare	3	9	12
Occasional	7	2	9
Frequent	2	1	3
Illness			
None to rare	7	9	16
Occasional	3	1	4
Frequent	2	2	4

TABLE 15

OROGENITAL ACTIVITY

	Male	*Female*	*Total*
Pre-illness			
None to rare	11	11	22
Occasional	1	1	2
Frequent	0	0	0
Illness			
None to rare	10	10	20
Occasional	0	1	1
Frequent	2	1	3

There was little change in the masturbatory activities among either the men or women (Table 14). Orogenital activity was rare in the pre-illness state and only 2 men and one woman admitted to frequent orogenital activity during their illness (Table 15).

Pre-illness libido was 3+ in 4 patients with none having 4+ libido. Libido during the illness was increased to 3+ or 4+ in 17 patients (Table 16).

Another important finding was the increase

TABLE 16

LIBIDO

	Male	Female	Total
Pre-illness			
0	1	3	4
1+	2	2	4
2+	7	5	12
3+	2	2	4
4+	0	0	0
Illness			
0	2	0	2
1+	0	2	2
2+	3	0	3
3+	4	5	9
4+	3	5	8

in libido or sexual desire in both sexes as compared with the actual sexual display. Seven of the 12 men (58%) were thought to have an increased libido of 3+ to 4+, but none of the 12 were classified as 4+ in their sexual display. Ten of the 12 (83%) women were thought to have an increase of their libido to 3+ to 4+ and 7 of the 12 (58%) had sexual display of 4+ (Table 17).

Discussion

The most striking finding in this study was the difference in sexual provocativeness of the male and female. A possible explanation for this is found in the statement of Deutsch[7] that "woman's sexual life remains more inhibited than man's." As a result it is more likely that "the hypomanic with his optimistic outlook is not so troubled by his conscience"[8] and will act upon his inhibited biologic drives. Supporting such an explanation is the data related to changes in libido when this is compared with provocativeness. It is apparent that men and women were nearly equally affected with increased libidonal drives (7 men and 10 women). There remained, however, the profound difference in provocativeness (0 men vs. 7 women). Further evidence is offered when the data is examined for the difference in provocativeness in men and women who had satisfactory pre-illness marital sexual adjustments. Here it may be observed that 40% of the women developed provocativeness whereas none of the men displayed such behavior.

TABLE 17

LIBIDO VS. SEXUAL DISPLAY

	Libido		Sexual Display	
	Male	Female	Male	Female
0	2	0	6	2
1+	0	2	3	0
2+	3	0	3	3
3+	4	5	0	0
4+	3	5	0	7

An objection to the preceding statements may be based on the observation that whereas 7 of the women in the study were either single, divorced, separated or widowed at the onset of their illness, only one man was separated. The serious limitations imposed on women obtaining sexual satisfaction when removed from their spouses, in contrast to the men, would be a possible determining factor. This could be interpreted to mean that satisfaction of sexual appetite in the pre-illness state resolves conflict so that during the manic phase, conflictual areas other than sex are more likely to be involved.

It should be noted that in this series the men tended to have a more severe manic reaction with 5 diagnosed as acute mania and one as delirious mania, whereas all 12 of the women were diagnosed as either hypomanic or manic. Thus one might say that the men were "too busy" or "too sick" to carry out any goal-directed activities such as provocativeness. However, it is interesting to note that none of the 6 men with milder forms of mania displayed any provocativeness.

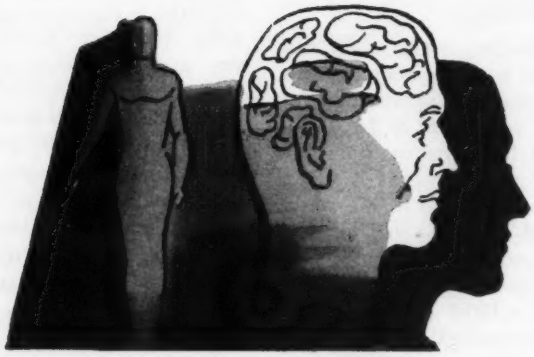
The finding that orogenital activity, mainly homosexual, was rare in our patients is in keeping with the statement by Bowlby,[9] that there "is little sexual perversion among cycloids but it is not at all unknown." Also, the observation of Rowe and Draggett[10] that the cycloid, in his pre-illness state . . . "is rarely (less than 10%) described as being . . . promiscuous" was borne out in our studies.

Since this is a preliminary report containing only 24 patients, general trends and tendencies were discussed. The authors intend to continue to collect data from additional patients in an effort to obtain a large series which will be more significant. Only in this way will the suspicions aroused in this preliminary report be confirmed or refuted.

References

1. Campbell, J. D.: Manic Depressive Disease. Philadelphia, J. B. Lippincott Company, 1953, p. 32.
2. Bellack, Leopold: Manic Depressive Psychosis and Allied Disorders. New York, Grune & Stratton, Inc., 1952, p. 17.
3. Noyes, A. P., and Kolb, L. C.: Modern Clinical Psychiatry. Philadelphia, W. B. Saunders Company, 1958, p. 356.
4. Davidson, G. M.: Manic-Depressive Psychosis: Theory and Practice, J. Nerv. & Mental Dis. 125:87, 1957.

5. Kinsey, A. C., Pomeroy, W. B., Martin, C. E., and Gebhard, P. H.: Sexual Behavior in the Human Female. Philadelphia, W. B. Saunders Company, 1953, p. 641.
6. Hollingshead, A. B., and Redlick, F.: Social Class and Mental Illness. New York, John Wiley & Sons, Inc., 1958.
7. Deutsch, H.: The Psychology of Women. New York, Grune & Stratton, Inc., 1944, p. 185.
8. Campbell, J. D.: *op. cit.*, p. 31.
9. Bowlby, J.: Personality and Mental Illness. New York, Emerson Books, 1942.
10. Rowe, C. J., and Draggett, D. D.: Prepsychotic Personality Traits in Manic-Depressive Disease, J. Nerv. & Ment. Dis. 119:412, 1954.



Complications of Pressor Amine Therapy*

EDWARD R. DORNEY, M.D.,† *Atlanta, Ga.*

The pressor amines have been a useful and welcome addition to the physician's armamentarium. However, as with other potent drugs, certain untoward reactions or side effects may occur. These emphasize the need for careful evaluation of the patient for the indications for their use, and the need for meticulous technic in their administration.

TREATMENT OF SHOCK in conditions other than blood loss has undergone considerable change in the past ten years. Prior to this time therapeutic efforts were directed mainly toward increasing intravascular volume by infusion of blood products and various other substances. In myocardial infarction, digitalis had been used in "cardiogenic" shock in an attempt to raise pressure by increasing contractile force of the heart. There had been use of epinephrine and phenylephrine HCl (Neo-Synephrine) in shock states. It was early in 1950 that pressor amine therapy of shock became important with the introduction of norepinephrine on the commercial market. In quick succession after this, mephentermine (Wyamine), metaraminol bitartrate (Aramine), methoxamine HCl (Vasoxyl) and several other preparations have appeared. All have their special benefits and all also have their toxic manifestations.

The beneficial effect of these drugs is unquestioned. This paper concerns itself with the toxic effects of the various pressor amines: the arrhythmias, local tissue damage and the ability of these amines to produce a shock-like state.

Not all of the difficulty seen with the materials is actually due to the drugs themselves, but quite often to a lack of understanding of the drugs by the medical personnel employing them.

Tissue Necrosis

Probably the best known complication of pressor amine therapy is that of tissue necrosis. There have been many cases of necrosis and slough of tissue reported due to subcutaneous leakage of norepineprhine infusions. The usual history is that an intravenous needle had become displaced with subcutaneous extravasation of the infusion. The affected limb becomes swollen and boggy but seldom shows any warning sign other than a mild decrease in temperature. The fluid is absorbed and all seems well. About 12 hours later the area appears blanched and dry. This progresses in a period of hours to redness with bullous formation and into areas of blackened necrotic tissue that become infected and slough away. It is interesting to note that McGinn and Schluger[1] were unable to produce consistent tissue necrosis by subcutaneous injection of undiluted 0.1% levarterenol in rabbits, but that tissue necrosis could be produced by continuous subcutaneous infusion of a much more dilute solution. They also found that the duration of infusion had to exceed one hour before appreciable results could be obtained. Their conclusion from these experimental data in rabbits was that the extent of damage caused was a function of the time of exposure of the tissue to the norepinephrine rather than to the total amount introduced or to the concentration of the drug used.

It has been our experience and that of others that tissue necrosis may occur following infusion with norepinephrine in the absence of any demonstrable infiltration of the subcutaneous tissue. The point of slough is usually located at or just distal to the needle point or catheter tip, but on occasion has been found well above the distal end of the intravenous catheter. Reactions of this sort have usually followed prolonged use of vasopressor substances over several days, or the use of highly

*Read before the Section on Medicine, Southern Medical Association, Fifty-Third Annual Meeting, Atlanta, Ga., November 16-19, 1959.

†From the Department of Medicine, Emory University School of Medicine, Atlanta, Ga.

concentrated solutions over shorter periods of time. The shape of the devitalized area of tissue has been roughly that of an ellipse and would correspond nicely with the area of destruction which could be expected from a mechanism as described by Shapiro and Perlow.[2] Studies in the isolated femoral vein of the dog by these authors have shown that seepage through the intact vein wall does indeed occur. It is understandable then that the stagnation of the norepinephrine infusion, whether due to previously existing phlebitis or to vasoconstriction caused by the drug itself, could supply sufficient concentrations of the drug over a sufficient period of time to cause death of tissue.

Extreme constriction of the infused vein may occur even in the absence of blanching of the surrounding tissue. This constriction is often mistaken for thrombophlebitis with the result that the infusion or cut-down is moved and local and systemic treatment for supposed phlebitis begun.

Actual thrombophlebitis may also occur due to norepinephrine, both in the infused veins and in the surrounding veins. This latter phenomenon is thought to be due to retrograde flow of the norepinephrine infusion into collateral channels because of elevation of the pressure in the main venous channel.

Recently we have had experience with a case of tissue necrosis due to infiltration of a solution of metaraminol (Aramine).[3] This occurred in a 60 year old man who was admitted because of a cerebrovascular accident. He was found, in addition, to have generalized atherosclerosis with almost complete absence of the pulses of the lower extremities. He had received some 40 intramuscular injections of Aramine in his well-vascularized upper extremities without mishap. He had also experienced a single episode of subcutaneous infiltration into the right arm which produced no difficulty. Following this the infusion of Aramine was started again in the right lower extremity to facilitate nursing care. A later episode of subcutaneous infiltration in the lower extremity resulted in an area of tissue necrosis and slough along the course of the greater saphenous vein. This case is particularly interesting since the agent used has not previously been reported as a cause of tissue necrosis, and because previous subcutaneous infiltrations in the well-vascularized areas of the same patient had been harmless. We believe this case points up the danger of the use of any potent vasoconstrictor in the presence of an already impoverished arterial circulation.

Arrythmias

Another less well-appreciated toxic effect of the pressor amines is their ability to produce arrhythmias. It was originally thought that norepinephrine had a lesser tendency toward production of arrhythmias than did epinephrine, that the production of bradycardia was its only effect on the heart, and that this effect was mediated through the vagus. Littler and McKendrick[4] showed that in dogs and monkeys norepinephrine is capable of producing premature ventricular contractions and supraventricular arrhythmias at least as frequently as epinephrine. They also presented two cases of human myocardial infarction; one in which ventricular tachycardia could be produced by the infusion of norepinephrine and another in which multifocal premature ventricular contractions resulted from norepinephrine infusion. It must be remembered, however, that the blood pressure in the first case rose from unobtainable levels to 140/100 in two minutes. In this regard Hoffman and associates[5] have noted that in dogs in which vagotomy had been done there is a short but definite period of increased ventricular vulnerability when norepinephrine is infused rapidly. This action is produced directly on the myocardium and is not mediated through the autonomic nervous system. This vulnerable period during which the fibrillation threshold was lowered to nearly that of the previous threshold of a single ventricular response lasted for about one to three minutes. When the drug was infused slowly, even in the same concentrations, this period of increased vulnerability was not demonstrable.

Recently Gold and Corday[6] have discussed the beneficial effects of the various pressor amines on arrhythmias due to myocardial infarction with decreased peripheral blood pressure. They postulate that this anti-arrhythmic effect is mediated through increased myocardial perfusion secondary to increased coronary filling pressure at the aorta and have reported the reversion of many ventricular and supraventricular arrhythmias. In one report, a case of supraventricular tachycardia following my-

ocardial infarction was treated with 5 mg. of metaraminol (Aramine) given intravenously. The blood pressure rose to 120 systolic where the supraventricular tachycardia converted to normal sinus rhythm only to be replaced by a ventricular bigeminy when the pressure reached 200/110. The bigeminy disappeared when the blood pressure again dropped to 140/90. Unfortunately, time intervals were not recorded as in Littler's cases so that analysis of the causation of the arrhythmia cannot be complete.

Miller,[7] in 1955, working with healthy young male volunteers and using a dilute solution of norepinephrine showed that five of nine subjects developed a supraventricular arrhythmia, predominantly A-V dissociation when hypertension was induced. He postulates, as have others, that increased vagal tone may be responsible for this arrhythmia and suggests that atropine be used as protection. Doses used in his studies were in the range of 1/150th grain given intramuscularly with resultant abolition of the A-V dissociation.

We have had experience with a single patient who was inadvertently given 1 mg. of atropine intravenously during a norepinephrine infusion. The resultant sinus tachycardia of 210 beats per minute was thought to be due to complete vagal block occasioned by this dose of atropine and would not contraindicate the use of the smaller doses intramuscularly or subcutaneously.

It is important to realize that not all of the vasopressor drugs have a definite arrhythmia producing potential. Drugs such as Vasoxyl and Neo-Synephrine are almost devoid of this ability. Their primary effect upon the heart is a reflex bradycardia mediated through the aortic and carotid pressor receptors through their ability to cause peripheral vasoconstriction. This particular peculiarity of these drugs has been used therapeutically in the treatment of paroxysmal auricular tachycardia.

The third major difficulty with the pressor amines is twofold: (a) the ability to produce a state which simulates shock during administration and (b) the period of hypotension which may follow withdrawal after a prolonged infusion.

A classical example is presented in the following hypothetical case:

A postoperative patient is found to have a blood pressure of 90/70 after having responded fully from anesthesia. He has no tachycardia and is not sweating or restless. The preoperative blood pressure was 110/70 but this is buried in the chart and unrecognized by the rounding intern. An infusion of pressor amine is started and the systolic pressure is raised to 110. With the rise in pressure there is a profound peripheral vasoconstriction accompanied by sweating, and now the patient fulfills the clinical picture of the shock state. It is noted that the longer the infusion is maintained the more pronounced is the vasoconstriction, and also it is noted that larger and larger doses of pressor amines are needed to maintain the blood pressure at the desired levels. Finally, when the diagnosis is doubted, the pressor amine is stopped and there is a sudden drop in the blood pressure to below pretreatment levels which further confirms the original faulty diagnosis of shock. This hypothetical case presents several of the potential dangers of the pressor amine therapy.

Indications and Use in Therapy

The primary fault cannot be attributed to the pressor amines themselves but to a fairly widespread error which has resulted from the introduction of this easily available method of treatment for shock. It must be remembered that the shock state is a clinical syndrome of hypotension, tachycardia, small pulse pressure, peripheral collapse, pallor, sweating and restlessness. In the majority of cases, the syndrome is complete or nearly so. Hypotension alone does not indicate shock and the level of blood pressure must be carefully evaluated for each individual. Postoperative hypotension, particularly, is most often due to hemorrhage or anoxia. Norepinephrine is capable of raising the peripheral pressure in either of these circumstances for a short period. The danger is that it may, by creating a false sense of security, mask the underlying lesion until it becomes irreversible.

All of the potent pressor amines are powerful vasoconstrictor agents and derive the greater part of their pressor abilities from this peripheral action. It is this action which produces the cold and pale extremities described in the hypothetical case and also induces peripheral sweating. The picture then, in this previously mildly hypotensive individual, has become one of shock with sweating, pallor and assisted blood pressure.

It has been our experience that patients treated with norepinephrine or Aramine for prolonged periods require increasing concentration of the materials to maintain blood pressure at the desired levels. This particular

phenomenon is well known to physiologists and has been reported for norepinephrine by Duner and Von Euler.[8] It can readily be seen, then, that in the patient who is cold, clammy, with severe peripheral vasoconstriction, and who begins to require larger doses of pressor amine to maintain his blood pressure, that the diagnosis of shock will seem to have been confirmed.

Finally, when it has been decided that perhaps this man is not in shock and that all of these peripheral manifestations are due to pressor amines, the infusion is suddenly stopped. When this happens the blood pressure drops precipitously to below the pretreatment level and the erroneous diagnosis again receives confirmation since this man is truly unable to maintain his blood pressure without the pressor amines.

It has been noted by many observers that when infusions of potent vasoconstrictors are suddenly discontinued there follows an immediate drop in blood pressure and which may be prolonged for several hours. The actual cause of this event is not known. Duner and Von Euler[8] have demonstrated in cats infused with norepinephrine for periods of 20 minutes or more that when the infusion is suddenly discontinued there follows a primary drop in pressure to below pretreatment levels and a secondary hypotensive state which persists for one to two hours. The actual mechanism of this drop is not fully understood but when an autonomic blocking agent such as TEAB is given to these animals the secondary fall of pressure can be eliminated but the transitory initial drop remains. It has been our experience in humans that if the drug is gradually discontinued as the pressure becomes self-sustaining, this drop can be eliminated. This has not been so in all cases, however, and it is sometimes helpful to use intramuscular metaraminol while the infusion of norepinephrine is being slowed and immediately after cessation of the infusion until the blood pressure has become stabilized.

There are many other difficulties in the choice of pressor drugs because of their variable sites of action. Drugs such as norepinephrine and Aramine have both a central action in increasing the force of ventricular contraction and a peripheral vasoconstrictor effect, both of which may contribute to their pressor abilities. Gazes[9] has shown that these drugs are capable of the elevating blood pressure of patients in shock due to myocardial infarction where phenylephrine HCl has been unsuccessful. The implication here is that the drugs with the cardiotonic action are more desirable in the treatment of shock due to myocardial infarction than those with a purely peripheral action, since with the latter group the damaged myocardium would be forced to work against an increased peripheral resistance without additional aid. It must be remembered, however, that these drugs are capable of producing arrhythmias in normal as well as in damaged hearts and that decision for their use should not be made lightly.

Gazes[9] has also demonstrated that congestive failure secondary to myocardial infarction in the presence of shock responded to norepinephrine and, in the same patient phenylephrine HCl (Neo-Synephrine) had been unsuccessful.

Our present practice in myocardial infarction is to first attempt to raise the blood pressure with intramuscular metaraminol in order to avoid the infusion of extra volume into an already overtaxed vascular system. If this fails, then slow infusion of a concentrated solution of either norepinephrine or metaraminol is used.

The requirements will be reversed, however, in selection of a drug for the treatment or prevention of hypotension due to spinal anesthesia. In this case, where the central pumping mechanism is intact and the defect is one of peripheral collapse, it would be logical to choose the peripherally acting drug such as phenylephrine HCl or methoxamine (Vasoxyl). The arrhythmia-producing potential of these drugs is extremely small, their bradycardic effect being mediated through the carotid and aortic reflexes secondary to the rise in pressure.

It has been suggested that peripherally acting drugs such as Vasoxyl and norepinephrine should be used in shock due to pulmonary embolus.[10] Since it has been demonstrated that drugs such as levarterenol bitartrate (Levophed) and Aramine are capable of raising the pulmonary artery pressure and could theoretically, if not practically, aggravate the cor pulmonale secondary to the pulmonary embolus. Here again there are not sufficient studies regarding the comparative

ability of these drugs to raise pulmonary artery pressure and to stimulate the cardiac musculature. Both of these potentialities have been demonstrated separately.

Summary

In summary, it can be said that while there is no doubt the pressor amines are of aid in treatment of shock, it must be remembered however that they do have potential toxic effects which can be minimized through a knowledge of the individual drugs and their actions.

References

1. McGinn, S. T., and Schluger, J.: Skin Sloughs Associated with Levophed, Am. J. Surg. 92:594, 1956.
2. Shapiro, R. A., and Perlow, S.: Skin Necrosis Following Intravenous Use of Norepinephrine, Am. J. Surg. 92:566, 1956.
3. Dippy, Walter E., and Dorney, E. R.: Tissue Necrosis and Slough Produced by Metaraminol Bitartrate, J.A.M.A. 170:1647, 1959.
4. Littler, T. R., and McKendrick, G. S.: L-Noradrenalin in Myocardial Infarction, Lancet 2:825, 1957.
5. Hoffman, B. F., Siebens, A., Cranfield, P. F., and Brooks, C. C.: The Effect of Epinephrine and Norepinephrine on Ventricular Vulnerability, Circulation Res. 3:140, 1955.
6. Gold, H., and Corday, E.: Vasopressor Therapy in Treatment of Arrhythmias, New England J. Med. 260:1151, 1959.
7. Miller, A., Cheng, T., and Freedman, M.: Electrocardiographic Changes During Norepinephrine Induced Hypertension in Normal Man, Am. Heart J. 50:567, 1955.
8. Duner, H., and Von Euler, U. S.: Secondary Fall in Blood Pressure Following Noradrenaline Infusion in Cat, Acta physiol. scandinav. 38:355, 1957.
9. Gazes, P. C., Goldberg, L. I., and Darby, T. D.: Heart Force Effects of Sympathomimetic Amines as Basis for Their Use in Shock Accompanying Myocardial Infarction, Circulation 8:883, 1953.
10. Aviado, D. M.: Cardiovascular Effects of Some Commonly Used Pressor Amines, Anesthesiology 20:71, 1959.

Discussion (Abstract)

Dr. William C. McGarity, Atlanta, Ga. It is a distinct pleasure to discuss Dr. Dorney's paper on a subject in which I have been particularly interested. He has given a concise review of the complications of pressor amine therapy, and I would like to discuss a few phases of the prevention and treatment of the local tissue complications.

The value of vasopressor agents in the treatment of patients with certain types of shock has been widely recognized. Levarterenol (Levophed), metaraminol (Aramine) and mephentermine sulfate (Wyamine) are useful in the treatment of shock caused by myocardial infarction, bacteremia, or hypersensitivity reactions and usually provide a favorable effect against neurogenic shock. The use of vasopressor drugs in the treatment of hypovolemic shock is only occasionally justified.

If proper precautions are not carried out, tissue sloughs may be caused by any vasopressor drug potent enough to be effective in the treatment of severe hypotension.

Any patient receiving vasopressors, particularly by the intravenous route, should not be left unattended and should have constant nursing supervision.

The choice of the pressor drug depends on the severity and duration of the shock. The less potent drugs, mephentermine and metaraminol, cause less local tissue damage, and should be used in the milder form of shock. These drugs can be injected by intravenous, intramuscular, or subcutaneous routes without additional fluid vehicle. If necessary, a continuous infusion of metaraminol, with a dosage up to 500 mg. per liter of fluid vehicle, may be administered. If the patient does not respond in a relatively short period of time with the use of mephentermine or metaraminol, then levarterenol—the powerful pressor antidote for shock—is the next drug of choice. With the use of continuous intravenous levarterenol, there is a need for a large quantity of fluid vehicle. The amount of fluid vehicle will depend on many factors.

In an emergency, the vasopressor may be started in any vein available. Leakage around the needle should be avoided, because extravasation of a potent pressor drug may cause local ischemia and sloughing. If continuous intravenous administration of the vasopressor drug is required for any length of time, the insertion of a polyethylene tubing into the vein is necessary.

Most cases of slough have occurred in the lower extremities; although they may occur on the dorsum of the hands and in the antecubital fossa. It is postulated that in the lower extremities necrosis probably develops because the legs are so frequently the site of arterial and venous disturbances, particularly in the elderly patient. With these conditions the rate of blood flow is reduced and stasis of the pressor drug occurs. Also, patients receiving pressor drugs are usually in shock and suffer from impaired peripheral circulation, thus local circulatory insufficiency is even more prone to develop. Therefore, leg veins below the knee and hand veins should be avoided as sites for continuous infusion of vasopressors.

Since increased permeability of the vessel is another factor in extravasation of the pressor drug, the polyethylene tube should be inserted into a large vein. This permits more dilution of the solution and less venous spasm. Sites where there is stagnation of blood should be definitely avoided.

The preferred site for insertion of a polyethylene tube for infusion of a potent pressor agent is the cephalic vein, with the tube threaded for several inches up into the axillary vein. The next best site is the femoral vein, with the polyethylene tube threaded into the iliac vein or vena cava. The tube should be tested with a solution of 5% dextrose and distilled water until a satisfactory flow is demonstrated. One must not force the solution in a vein that is in marked spasm. Elevation of the extremity aids venous return and prevents stasis of the solution in the vein. Occasional flushing of the vein with saline or with a 5% dextrose solution in distilled water also helps to prevent stagnation. If thrombosis occurs in the polyethylene tube, a fresh tube should be inserted at another site.

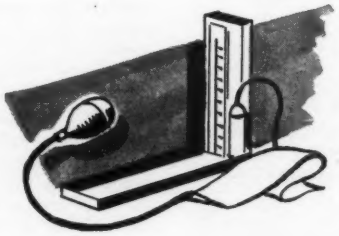
Another method of preventing ischemia and tissue necrosis from a potent vasopressor drug is by using a mixture of the pressor amine and an anti-adrenergic drug. Levarterenol and phentolamine (Regitine) in a ratio of 4 to 4 mg. up to 4 to 40 mg. per liter of fluid vehicle seems to be the mixture of choice in the treatment of severe shock. Phentolamine when added to levarterenol solution will antagonize its local vasoconstrictor action but not its systemic pressor effect. In this manner the ischemic effect from the extravasation

of levarterenol will be counteracted by simultaneous infiltration of the phentolamine.

Studies have demonstrated that solutions of levarterenol to which relatively large amounts of phentolamine have been added have a pressor effect equivalent to that of levarterenol alone. Phentolamine in doses of 10 to 40 mg. per liter does not decrease the pressor effect of 4 mg. of levarterenol. However, 60 mg. of phentolamine will decrease or abolish the hypertension produced by 4 mg. of levarterenol. Five mg. of phentolamine injected intravenously within a few seconds is sufficient to antagonize briefly the pressor effect of a slow drip of 4 mg. of levarterenol. A dose of phentolamine in an amount that does not decrease the systemic pressor effect of levarterenol will combat its local vasoconstrictor action. The recommended dosage of phentolamine is 5 to 10 mg. per liter with 5 mg. of levarterenol. This mixture will prevent tissue necrosis in most instances. In view of these facts, when levarterenol is used in the treatment of shock, it might be well to adopt the mixture of levarterenol and phentolamine as a routine procedure.

The treatment of ischemia of tissue caused by potent vasopressor drugs should be prompt. Meticulous observation of the site of infusion and frequent inspection along the course of the vein is necessary to detect the early pallor, cyanosis, or induration in time to avert irreversible changes in the tissue. If there is any evidence of ischemia, administration of the pressor amine at that site should be immediately discontinued and phentolamine injected into the area of tissue damage. When 5 to 10 mg. of phentolamine diluted in 20 cc. of water is infiltrated subcutaneously throughout the area of ischemia, the pallor and coolness disappears in most cases within 5 to 7 minutes. If ischemia remains untreated, extensive necrosis may develop. Hot packs should not be applied to the area of tissue damage because their use increases the metabolic demands of the ischemic tissue.

If the treatment is not successful and sloughing occurs, a skin graft may be necessary. Occasionally, when the pressor drugs are not used properly, the ischemia of an extremity may be so extensive that an amputation is required.



Choice of Agents for Preoperative Preparation of the Colon*

ISIDORE COHN, JR., M.D.,† *New Orleans, La.*

The use of chemotherapeutic agents is a great aid in preparing the patient for colon surgery preoperatively. However, the several agents are not of equal efficiency and in fact some are apparently quite useless in this regard. Nor should these drugs permit a false sense of security in terms of premature operation or carelessness in operative technic. Certain dangers accompany intestinal antisepsis.

THE CHOICE OF AN AGENT for intestinal antisepsis should be based upon the knowledge that the chosen agent can satisfactorily answer three major requirements: (1) rapid and effective control of the bacterial flora of the gastrointestinal tract, (2) satisfactory prevention of the development or overgrowth of pathogenic organisms, and (3) possesses a low local and systemic toxicity, which includes having limited absorption from the gastrointestinal tract. Comparisons between studies of single drugs are difficult because of the differing circumstances under which each study is conducted. Thus we have been interested in the direct comparison of a number of drugs studied under standardized conditions in a single institution.

Over a period of five years we have studied some 30 different intestinal antiseptics and believe the studies permit direct comparisons among these agents.[1-6] All studies have been conducted upon hospitalized patients who had no known disease of the colon. All patients were placed upon a standardized low residue diet, a standardized program of mechanical cleansing, and upon the antibiotic of choice. Stools were obtained for quantitative aerobic and anaerobic bacteriologic analysis before the administration of antibiotic was begun, daily during the treatment, and for a brief period after completion of therapy.

On the basis of our studies of the reduction in bacterial flora, and on the basis of the requirements we have established for each drug, we have divided the various agents into those not recommended and those that are recommended as intestinal antiseptics (Table 1).

The drugs that are not recommended include all agents that fail to control the flora of the gastrointestinal tract. Obviously an agent that is not effective bacteriologically cannot be of any assistance in this field. Among the agents that should be particularly mentioned in this connection are the sulfonamides, the broad spectrum antibiotics, and Clorpactin. Even though the poorly absorbed sulfonamides are widely used as intestinal antiseptics, the studies here and in other places demonstrate that these agents are almost worthless for the control of the flora of the gastrointestinal tract.

Many of the common broad spectrum drugs are not recommended because they fail to control the flora of the gastrointestinal tract. Furthermore they are in such widespread general use that there is an increased danger of development of antibiotic-resistant organ-

TABLE 1

INTESTINAL ANTISEPTICS

Not Recommended	
Chloramphenicol	Sulfasuxidine
Chlorquinaldol	Sulfathalidine
Clorpactin WCS-90	Tetracyclines
Colimycin	Chlortetracycline
Erythromycin	Oxytetracycline
Furazolidone	Tetracycline
Novobiocin	Tetracycline V
Penicillin V	Tetracycline-Nystatin
Ristocetin	Thiostrepton
Recommended	
Amphotericin-neomycin	Polymyxin B-neomycin
Bacitracin-neomycin	Sulfathalidine-neomycin
Kanamycin	Thiostrepton-neomycin
Nystatin-neomycin	

*Read before the Section on Proctology, Southern Medical Association, Fifty-Third Annual Meeting, Atlanta, Ga., November 16-19, 1959.

†From the Department of Surgery, Louisiana State University School of Medicine, New Orleans, La.

isms in the gastrointestinal tract of the patient being prepared for colon surgery, where such a complication can be least afforded.

Another drug in this category is Clorpactin WCS-90, which can only be used by direct injection into the colon at the time of operation, since it cannot be given orally or systemically. It must be used in conjunction with some type of irrigation, since it is only effective when it is used in the absence of any fecal material.[7] Thus direct irrigation of the colon, with copious amounts of solution must be employed at the operating table for this drug to be effective. The danger of spillage during the extensive irrigation is sufficient to make this a hazardous undertaking. In a patient without obstruction proper preoperative mechanical cleansing should not be omitted, and in one with obstruction, the dangers of irrigating with large quantities of solution would increase the risk of perforating the distended bowel. Thus, Clorpactin presents more dangers than benefits.

In the group of drugs that cannot be wholly recommended must also be placed combinations of neomycin with erythromycin, chlorquinaldol, novobiocin, ristocetin, oxytetracycline, or tetracycline. Even though several of these combinations have been found to be most effective bacteriologically, they possess certain other properties which make them less desirable for intestinal antisepsis. The most important is that these are combinations of neomycin with another agent widely used in the therapy of systemic infections, and therefore each is likely to lead to the development of antibiotic-resistant organisms. Several of these are rapidly absorbed and therefore cannot exert their maximum effect in the colon where it is most needed. Finally, several of these agents are specifically recommended for the treatment of staphylococcal disease, and their use as a preoperative measure would limit their usefulness if staphylococcal complications developed in the postoperative period. These combinations would be of most value in those patients who have been on prolonged antibiotic therapy for other reasons and therefore would be more prone to develop staphylococcal complications in the gastrointestinal tract, or in those patients who had developed a frank postantibiotic staphylococcal diarrhea.

Neomycin alone must be placed in a unique category since it is superior to those drugs which cannot be recommended, but yet is not quite as good as the drugs to be discussed later. It is indeed a most useful agent, and until relatively recently was the only single agent that found any real favor as an intestinal antiseptic. However, it is now generally agreed that it is more effective in combination with certain other drugs, and therefore it cannot be placed in the same category as those which are fully recommended.

In the recommended group are the agents that are the most effective in the control of bacterial flora of the gastrointestinal tract, produce the least side reactions, and can be expected to provide the best results in preparation of patients for elective colon surgery. Since there is little absorption from the gastrointestinal tract, their action will be concentrated in the colon where it is most needed, there will be less likelihood of their being used for systemic infections, and there will be little likelihood of their producing any changes outside the gastrointestinal tract. There are two combinations of neomycin with antifungal agents. Both combinations produced better control of the bacterial flora of the colon than would be expected from the combination of neomycin with an antifungal agent, even though this observation cannot be explained. Many believe that the routine use of an antifungal is desirable and necessary to prevent the development or overgrowth of fungi during preoperative preparation. While this has not been our experience, except in infants where we *do* recommend an antifungal agent, there can be no real objection to the use of either of these agents since they do provide such superior control of the colonic flora.

With one exception, the remainder of the drugs are combinations of neomycin with some other agent. The choice between these various combinations should be essentially a matter of personal preference since their actions are so nearly comparable.

Kanamycin is the only single drug in this group, and we have recently come to accept it as the best agent for routine preoperative preparation of the colon.[1] Since July 1959, kanamycin has been the agent of choice for all patients subjected to elective colon surgery on our service. One reason is that kanamycin is as effective bacteriologically as almost any

of the combinations. It seems reasonable to believe that one should accept one agent in place of two whenever this is possible. Another reason is that kanamycin does not produce the diarrhea that is common with neomycin. Some believe this is a desirable characteristic of neomycin since it will aid in the cleansing of the colon, while we believe that cleansing of the colon should be accomplished by agents specifically chosen for this purpose. Finally, another desirable characteristic of kanamycin is that kanamycin can be injected in large doses into the peritoneal cavity without danger,[8] while intraperitoneal neomycin may produce severe respiratory depression. Kanamycin has been employed in over 40 cases during which time we have continued to be impressed by its action.

Clinical Experience

It was shown experimentally that the optimum protection of colon anastomoses placed under extreme stress could be provided by a combination of four factors: preoperative mechanical cleansing, preoperative antibiotic therapy, antibiotics placed in the lumen of the colon at the site of the anastomosis, and antibiotics injected directly into the lumen of the colon in the postoperative period through a small plastic tube inserted into the colon proximal to the anastomosis.[9] Following this experimental study, all patients coming to elective colon surgery on our service since July 1955, have been treated with this antibiotic program,[2] and the study now includes over 400 patients who have received one or more parts of this triphasic antibiotic routine. These patients have been subjected to all types of colon surgery, and the results are sufficiently encouraging to warrant continuation of the study. It appears that the complications have been decreased by this schedule of antibiotic therapy, though this has not been subjected to statistical analysis. Complications have not been eliminated by this program of antibiotic therapy, and it should never be expected that antibiotics will completely eliminate complications in a field as complex as that of colon surgery.

Dangers

A discussion of the importance of antibiotics in colon surgery would not be complete without some mention of the possible dangers that might occur with the indiscriminate use of these drugs.

One complication that has been accorded a large place in the thinking of many interested in this field has been the problem of diarrhea due to staphylococci, fungi, and even worse, to pseudomembranous enteritis or enterocolitis. It must be remembered that this condition was recognized before antibiotics were used, and that there must be inciting factors in its production other than the administration of oral antibiotics. Methods for producing this condition experimentally require a multitude of factors acting simultaneously.[10,11] Study of the flora of the stool has led us to believe that fungi are rarely if ever the cause of diarrhea that may develop in these patients, and therefore we have not been unduly concerned about this complication except in infants. When staphylococcal diarrhea does occur, it should be treated with one of the specific antistaphylococcal agents in conjunction with all supportive measures that may be necessary.

As more and more effective agents have been introduced, and as society has moved at an ever increasing pace, the urge to shorten the period of preoperative preparation has become more and more important. Some have advocated the shortening of this period to the time of operation alone, as with Clorpactin, while others have advocated shortening the period to a single 24 hour period. In our experience, this is totally undependable to produce bacteriologic control of the fecal flora, and therefore, is to be condemned on this basis alone. But even more important is the finding that adequate mechanical cleansing of the colon can hardly be obtained routinely within this short 24 hour period, and thus some of the important advances of the recent past in surgery of the colon would be sacrificed merely to expedite the performance of an elective procedure. Our large experience with drugs that do not produce satisfactory control of the fecal flora has demonstrated that mechanical cleansing does not control the bacterial content of the colon, even with the 5 day period of preparation used in some studies, and thus a single day of mechanical cleansing, whether with or without antibiotics, should not be expected to control adequately the flora of the colon. Antibiotics cannot control the flora of a large

mass of feces where the antibiotics cannot come in contact with the bacteria, and so adequate mechanical cleansing is of the utmost importance in the proper preparation of the colon.

Overreliance on antibiotic protection has led to the assumption that proper antibiotic coverage would permit technical steps which were condemned before the antibiotic era. Thus more and more has been written about one stage resection and anastomosis in the presence of colonic obstruction.[12,13] Such procedures have been performed safely for years in lesions of the right side of the colon. Most surgeons have hesitated to attempt this in the presence of obstructive lesions in the left colon because of the many different problems and the high associated mortality in operation in this area, until recently the antibiotics again stimulated interest in this field. Believing that such procedures carried an undue risk, we considered the problem in an experimental investigation and were able to demonstrate that the performance of a resection and anastomosis with antibiotic support in an animal with a week-old obstruction of the colon was associated with a mortality of 40%, while a colostomy could be done with no mortality.[14] Thus, there is experimental confirmation for the previously known dangers of performing such a procedure in the presence of a distended, obstructed colon. In the face of such risks there would seem to be little justification for adopting these procedures when even without antibiotics, safe procedures are still available to the patient.

If antibiotics aid in the spread of malignant disease of the gastrointestinal tract then there is further reason for caution in their use. Experimental work has suggested that sterilization of the colon may enhance the rate of metastases from a lesion of the colon.[15] This work is being repeated and enlarged to see if the conclusions reached in a small experimental study are valid for a large series. How safely one may transpose such information from the experimental laboratory to the clinical patient is not known, but the many variables in clinical cases of carcinoma of the colon make this almost impossible to study in the clinic.

Thus the choice of an intestinal antiseptic depends not only on knowledge about which agent will have the most effective antibacterial spectrum, but what other uses the drug has, whether or not there are dangers involved in the use of the antibiotic, and whether or not the antibiotic will be expected to perform beyond its natural capabilities.

Summary

The results of a comparative study of various intestinal antiseptics have been presented.

The agents studied have been divided into two classes depending on their efficacy as intestinal antiseptics.

The recommended drugs are kanamycin, or combinations of neomycin with amphotericin, bacitracin, nystatin, polymyxin-B, sulfathalidine, or thiostrepton. Clinical experience over a 4 year period with a triphasic program of antibiotic therapy in colon surgery now includes over 400 cases.

Some dangers of intestinal antisepsis have been outlined.

The value of properly used intestinal antisepsis is reaffirmed.

References

1. Cohn, I., Jr.: Kanamycin for Bowel Sterilization, Ann. New York Acad. Sc. 76:212, 1958.
2. Cohn, I., Jr.: Antibiotics for Colon Surgery, Gastroenterology 35:583, 1958.
3. Cohn, I., Jr., and Longacre, A. B.: Preoperative Sterilization of the Colon; Comparison of Various Antibacterial Agents, Antibiotics Annual 1955-1956:105, 1956.
4. Cohn, I., Jr., and Longacre, A. B.: Preoperative Sterilization of the Colon; Comparison of Various Antibacterial Agents. II. Antibiotics Annual 1956-1957:253, 1957.
5. Cohn, I., Jr., and Longacre, A. B.: Preoperative Sterilization of the Colon; Comparison of Various Antibacterial Agents. III. Antibiotics Annual 1957-1958:635, 1958.
6. Cohn, I., Jr., and Longacre, A. B.: Preoperative Sterilization of the Colon; Comparison of Various Antibacterial Agents. IV. Antibiotics Annual 1958-1959:761, 1959.
7. Gliedman, M. L., Grant, R. N., Vestal, B. L., Rogers, C. E., and Karlson, K. E.: Clorpactin, A Surgical Adjunct, Surg. Forum 8:104, 1957.
8. Cohn, I., Jr., and Beauclair, B.: Intraperitoneal Antibiotic Administration, Surg. Forum 9:204, 1959.
9. Cohn, I., Jr., and Rives, J. D.: Protection of Colon Anastomoses with Antibiotics, Ann. Surg. 144:738, 1956.
10. Menaker, G. J., and Van Hagen, F.: An Evaluation of Distention and Stasis in the Pathogenesis of Experimental Pseudomembranous Enteritis, Surg. Gynec. & Obst. 108:409, 1959.
11. Tan, Toh-Leong, Drake, C. T., Jacobson, M. J., and Van Prohaska, J.: The Experimental Development of Pseudomembranous Enterocolitis, Surg. Gynec. & Obst. 108:415, 1959.
12. Ferguson, W. H., and Chase, W. W.: Emergency Definitive One-stage Surgery for Intestinal Obstruction, M. Ann. District of Columbia 26:61, 1957.
13. Windsberg, E.: Intestinal Obstruction of the Distal Colon Due to Malignancy: Single-stage Decompression and Resection, Surgery 46:305, 1959.
14. Atik, M., Castleberry, J. W., Werner, J. C., and Cohn, I., Jr.: Primary Anastomosis of the Obstructed Colon: An Experimental Study, Surg. Gynec. & Obst. (In Press).
15. Vink, M.: Local Recurrence of Cancer in the Large Bowel; Role of Implantation Metastases and Bowel Disinfection, Brit. J. Surg. 41:431, 1954.

Exaggeration of Symptoms, Malingering, and Conversion Reaction*

ARTHUR M. PRUCE, M.D., MAURICE L. B. CLARKE, M.D., and HENRY J. CLIMO, M.D., *Atlanta, Ga.*

The subjective complaints are evaluated, and their management considered from a multidisciplinary approach.

Part I

THE PATIENT with a musculoskeletal disability who appears to be persistently disabled in the face of adequate and purposeful physical treatment, and who fails to return to work in the time usual for such disability, may have an unrecognized functional disorder.

That simulated disease is a worldwide problem is evidenced by a recent report by Soviet physicians who describe an investigation whose aim it was "to fix the threshold of hearing by means of pneumographic registration of respiratory movements. It was found that noise, light, and pain stimuli lead to alteration in the rhythm of respiratory movements. At the first perception of sound, respiration is either slowed down or accelerated, and when repeated, the respiratory rhythm is unaffected." The Russian authors believe that the procedure can detect true deafness and differentiate it from simulated deafness.[1]

The failure of sound conservative treatment is an indication for diagnostic re-evaluation; the patient's emotional state is cautiously explored and the probability of symptom exaggeration, malingering or conversion reaction considered. Apparently, difficulties face the conscientious physician in the diagnosis of these three, and there is no general agreement as to the best methods for evaluating exaggeration of symptoms, unmasking the malingerer, or diagnosing conversion reaction. The hesitancy with which these diagnoses are made is due to our approach to our patient. We assume that his complaints are genuine, his troubles real, his story true, and that he is sincerely seeking our aid and comfort.

Yet, the problem patient in whom good treatment has failed to relieve symptoms of musculoskeletal disease or injury, or in whom symptoms have recurred, is difficult to evaluate. Pinning a premature diagnosis of hysteria or malingering on organic disease can well be embarrassing for the physician, and confusing and upsetting for the patient. The patient is then often confronted with frequent examinations, multiple therapeutic suggestions, and his complaints are given "deaf ear" treatment. In the presence of an undiagnosed organic lesion, psychiatric consultation is worthless.

However, if the diagnosis of functional disease is missed, physical treatment will fail; the physician is frustrated; the insurance carrier is out his funds; and the patient's concept of his disease is reinforced and fixed, and his illness pointlessly prolonged.

Some degree of exaggeration of symptoms is to be expected in all patients. Such patients are honestly convinced they are sick, symptoms are described in superlatives; severity, intensity, and duration are alleged to be prolonged and continuous, and often claims are made of the failure of analgesics, narcotics, and physiotherapy to relieve pain and discomfort.

To differentiate between these three, the concept is offered that everybody exaggerates a little bit, though the malingerer is aware of the dishonest motives behind his symptoms whereas the patient with conversion hysteria is not.

Whenever the question of compensation arises and some monetary and/or interpersonal gain enters the picture, malingering enters into the differential diagnosis as in:

1. Disability and hospitalization insurance,
2. Disability payments under Workmen's Compensation Acts,

*Read before the Section on Physical Medicine and Rehabilitation, Southern Medical Association, Fifty-Third Annual Meeting, Atlanta, Ga., November 16-19, 1959.

3. Social Security, its premature enjoyment (at age 52 the patient can begin to draw disability insurance benefits if disabled instead of waiting until 65),

4. Litigation for injuries sustained in accidents (professional malingerers),

5. Military: physical examinations for promotion-retirement, "gold-bricking" and riding the sick-book.

Forms of fraudulent behavior:

1. Shamming injury at work,
2. Self-inflicted injury,
3. Dissimulation/simulation,
4. Exaggeration/aggravation.

Unmasking fraudulent behavior—primary evidence:

1. Spontaneous confession,
2. Denunciation by co-worker,
3. Eye witness,
4. Discovery of object or device used to inflict injury.

Character of malingerer—sources of information available:

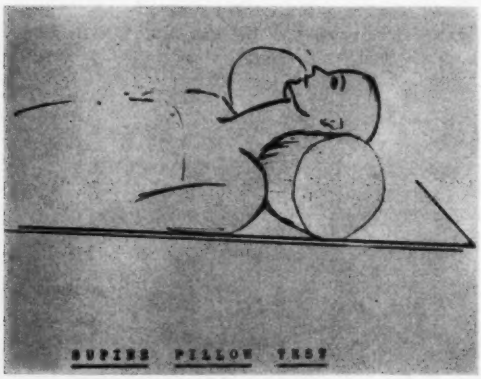
1. Red Cross or Social Service section,
2. Insurance company records,
3. Army records,
4. Court records, digest of court cases,
5. V.A. records—service connected disability,
6. History of alcohol—the index of suspicion is greater.

The great hesitancy shown in committing ourselves to this sensitive diagnosis is due to the fact that proof of intent in the malingerer is difficult to confirm medically and almost impossible legally. However, where a discrepancy exists between a patient's complaints and the clinical findings, testing for malingering is indicated.

Malingering must be ruled out when:

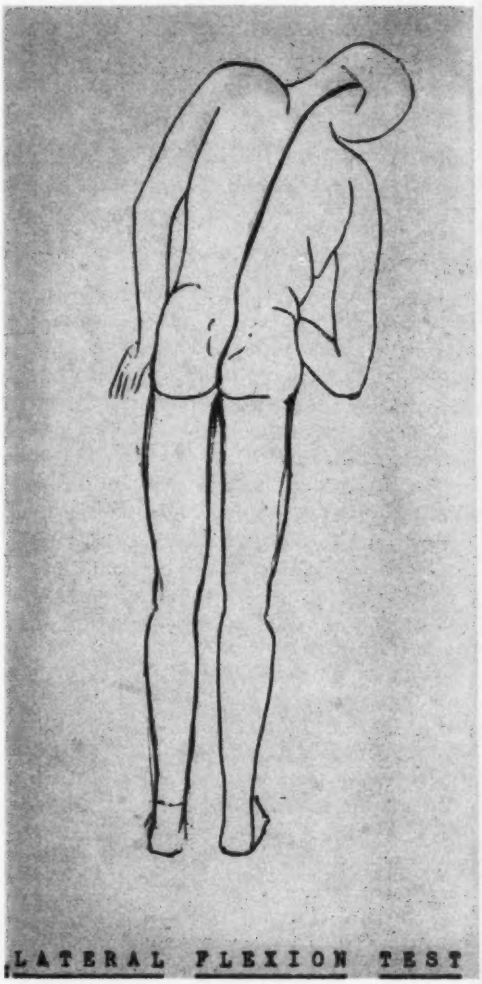
1. Disability is out of proportion to the injury,
2. Persistent pain is out of proportion to the original lesion,

FIG. 1



Simulated stiff neck.

FIG. 2



3. Prolonged recovery period beyond that usual for similar disorders,

4. Subjective complaints with few or no objective findings.

The most frequent complaints relate to pain, stiffness, weakness and rarely numbness. My favorite tests for malingerers are:

Neck.

Stiff neck. Patient can't move it, and defends himself against all passive movements. Supine test—voluntary nature of the immobile neck is evident (Fig. 1).

Back.

(1) *Two-table test*—discreetly observe the patient as he gets on and off the examination table, and then on and off the x-ray table. The patient who is

simulating stiffness of the back will often relax after completion of his physical examination and functional ranges of motion are demonstrable as he gets on and off the x-ray table.

(2) *Lateral flexion test*—will consistently reveal muscle spasm and restriction of motion if a significant disability is present (Fig. 2).

(3) *Dropped pants test*—stiff back is found on examination, but agility on pulling pants up (Fig. 3).

(4) *Deyerle-May sciatic tension test*—The malingerer is often acquainted with the supine straight leg raising test and will do the appropriate grunting and groaning with his leg just a few degrees off the table. Deyerle and May have described a sciatic tension test that aids in differentiation of the pain of nerve root compression from other causes of low back pain with the patient seated.[2] "Patient seated, legs dependent, body erect; the knee is slowly passively extended until patient indicates when the pain is reproduced. The knee is then flexed to a point just below the threshold of pain, and with the leg locked between the examiner's knees at the sub-pain level, pressure applied over the sciatic nerve in the popliteal space will apply tension on nerve, and pain is reproduced in the back or leg or both (Fig. 4).

Where malingering is suspected, one reverses the procedure and does not press on the sciatic nerve but instead presses very firmly over the patella. If this reproduces the sciatic pain, it would be evident that the patient is stretching the facts considerably further than the examiner is stretching his sciatic nerve roots."

FIG. 3

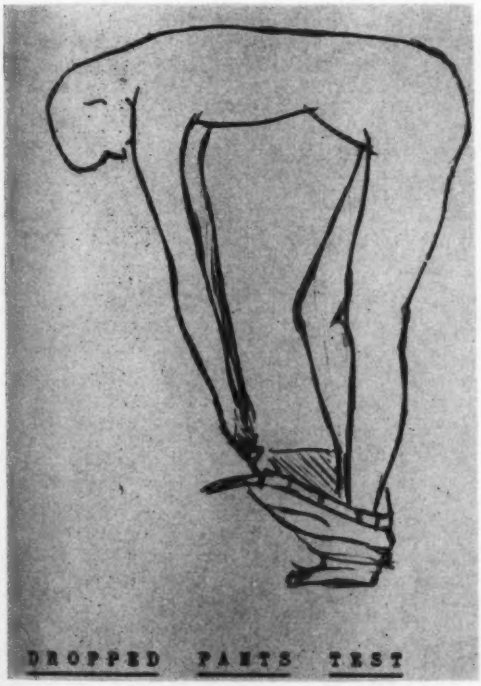


FIG. 4

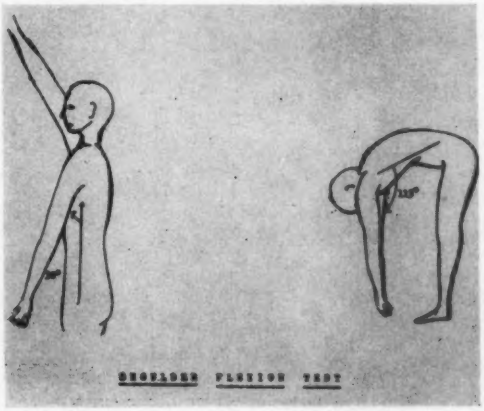
With the leg locked between the examiner's knee at the sub-pain level, pressure is applied over the sciatic nerve in the popliteal space. In a positive case, pain is reproduced in the back or leg, or both. (Deyerle and May, Sciatic Tension Test, South. M.J. 9:999, 1956.)

Upper Extremity.

The patient who simulates *stiffness of the shoulder* that limits motion of the shoulder joint to considerably less than a right angle, can in the course of the examination of his back be asked to touch his toes, and unwittingly uncovers a range of motion of the shoulder joint that is functional (Fig. 5).

Grip strength—in injuries of the fingers and hand, the evaluation of grip strength by comparing dynamometer readings of the normal hand against injured

FIG. 5



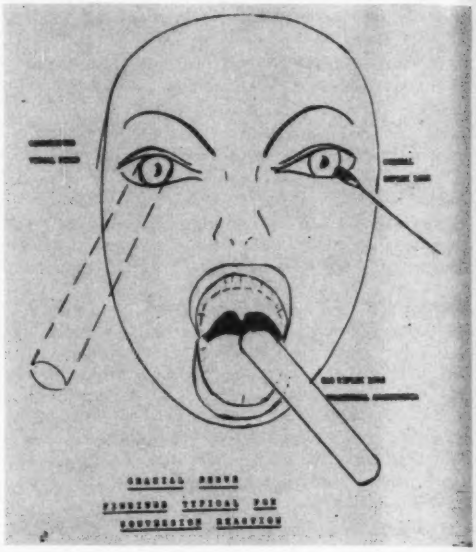
hand is worthless in the patient who simulates tremendous effort without exerting any appreciable grip. To detect the malingerer, the Jamar Adjustable Dynamometer with dial is used, grip testing normal and injured hands as usual, and the patient is permitted to see the dial readings for both hands[3] (Fig. 6). Grip test is repeated after a five minute interval but the patient is not shown these dial readings. There will be less than a 10% variation in strength test if the patient has fully exerted himself; in the malingerer who exerts less than full effort, variations of 20 to 100% on repeat testing may be recorded. Basic is the fact that it is almost impossible to grasp at less than maximum effort and then reproduce this effort exactly after a lapse of a few minutes.

There is no sharp dividing line between the fraudulent malingerer and the patient with conversion reaction. Both the malingerer and the conversion hysteria patient report symptoms of illness or disability in situations where such illness serves either as a means of avoiding an unpleasant consequence or of receiving profit. The mechanism and its results are much the same in both cases; however, the conversion hysteria patient is not conscious of his maneuver and hence actually feels the pain or disability.

FIG. 6

Grip strength testing—Jamar Dynamometer.

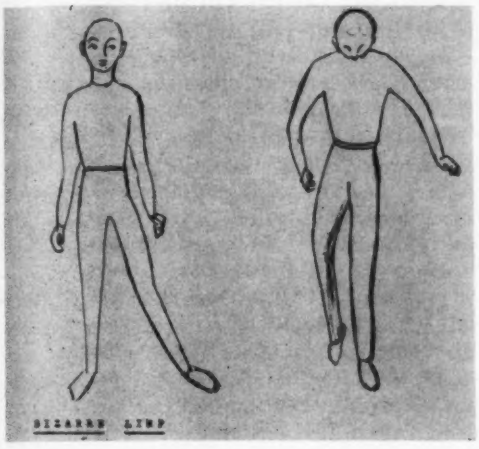
FIG. 7



Tests for Conversion Reaction: Since the hysterical patient uses his extremities for expression of his unconscious emotional needs, cranial and peripheral nerve pathways must be evaluated. A so-called "hysterical anatomy" is a consistent finding in such patients, and if

FIG. 8

FIG. 9



cautiously searched for can be readily demonstrated. Also obvious questioning can induce such evidence, which can be of diagnostic significance.

Typical hysteria—cranial nerves (Fig. 7):

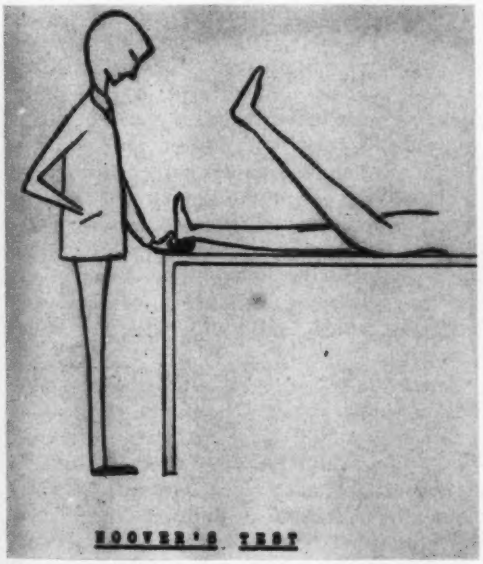
1. corneal anesthesia, tested by soft cotton applicator;
2. constricted visual field, to tubular vision;
3. pharyngeal anesthesia, by use of tongue blade.

Hand—paresis in bizarre posture (Fig. 8).

Leg—paresis in bizarre posture, a limp (Fig. 9).

Leg—Hoover's sign—the heel thrust absent in true paralysis (Fig. 10).

FIG. 10



Sensory—the pattern in loss of sensibility in the conversion syndrome is remarkable in that the anesthesia surrounds the limb, often at the level of a joint, and all forms of sensibility to this level are affected. A sharp line of demarcation between sensation and its loss is always suspect. If loss of sensibility and paresis are bizarre, galvanic-faradic studies that demonstrate normal motor responses are proof of conversion hysteria (Fig. 11).

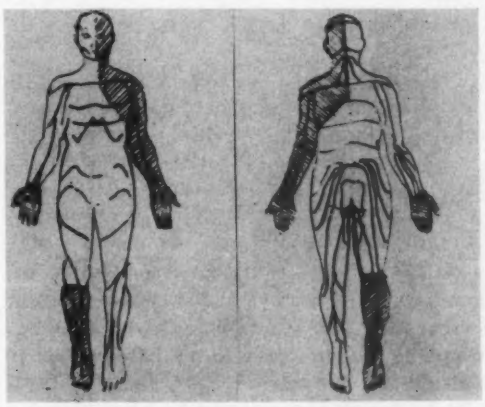
In conclusion, when the examination is suggestive of functional disorder, the diagnosis can be confirmed by these simple tests and are to be considered as positive findings.

Part II

(M. L. B. Clarke, M.D.) The reaction to injury, without taking up the problem of psychoneurosis and its mechanisms, is either physical or mental, according to the patient's personality. Each of these responses is affected or modified by accompanying circumstances. The response to injury is conditioned by the anxiety of the patient about his future and that of his dependents, and by the influence extended upon him by his immediate associates and family, and may be later further influenced by other factors, such as litigation and its possible enhancement.

The back is a favorite area for escape from an intolerable life situation; this is true because: (1) backache is frequently a result of or associated with injury or the results of occupational and postural fatigue; (2) the association in the lay mind of backache with kidney disorders (the adequacy of backache, either real, exaggerated or assumed, as a focal release from unpleasant or disagreeable duties

FIG. 11



Patterns of anesthesia in functional disorders.

and responsibilities); and (3) the tendency of mental tension and nervousness to manifest itself in the back as that part of the body most subject to mechanical stresses and fatigue.

It is scarcely necessary to detail all of the physical signs of true lesions of the back, as they are so well known to every physician of experience. However, failure to find these, or at least one or more of them, is strong evidence of a psychic or malingering origin of the complaint. Included in the most reliable of the diagnostic signs to be searched for are: (1) deformity, (2) muscle spasm, (3) muscle imbalance or weakness, (4) localized points or pressure signs of tenderness, (5) limitation of motion, and (6) x-ray findings.

The definitive signs associated with organic lesions of the back are difficult to simulate or even to exaggerate, either voluntarily or subconsciously, and an attempt to do so will result in bizarre performances. Deformity may be due to destructive bone lesions, fracture, or dislocation. Muscle imbalance may be caused by any of the above, plus the effect of an increase or loss of muscle tone.

X-ray findings may supplement, confirm, or at times, determine the correctness of the clinical diagnosis.

Localized tender pressure points, if they extend beyond the anatomic borders of the involved tissues, if they fail to reappear consistently during the examination, if the patient cringes before pressure is applied, or if the patient fails to respond to pressure when his attention is distracted, then the patient should be suspected of malingering. Even in the hysterical patient, while these pressure points may be bizarre and not conform to anatomic borders, they at least, will be consistent.

Tactile sensation in the back is not critical as it is in the forearm or a finger, and responses to pinprick will vary. Back movements are painful and restricted in those areas which affect the movement of the involved part, but in the malingerer movements are apparently affected and painful even in such adjacent parts that physiologically cannot affect or influence the involved area. In other words, the exaggerator restricts movement in *all* directions and in joints that do not affect the area claimed to be injured. He resists passive movements that should be painless and inadvertently performs movements without difficulty which would affect the same group of muscles if true disease were present. For example, he may resist flexion of the hips while lying supine and then sits up in a chair without difficulty while putting on his shoes.

Torsion curves of the back are difficult to maintain over long periods of time, or to duplicate time after time during the process of the examination; hence it is well to repeat this part of the examination at least once during the interview.

There is one type of patient of particular interest. This is the *dissimulator,* the patient who attempts to use the evidence of an old injury for his gain, and which he has previously concealed during the pre-employment examination. It is incumbent upon the industrial physician to ferret out this type of person and expose him. Remember that the effect of dissimulation is to make the employer or his insurance carrier financially responsible for aggravation or exaggeration of *any* pre-existing condition, once he hires the man. The courts have held, time after time, that an employee may *not waive* his personal rights; this is particularly true of the State Board of Workmen's Compensation, and this often encourages a prospective employee to attempt to hide a disability at the time of his employment. Once hired, his entire body becomes subject to the ravages of real or fancied effects of trauma.

One of the peculiarities of the human personality manifests itself in denying any and all pathologic states when it is expedient to do so, such as at the time of hiring or promotion, and this same individual may conjure up any conceivable condition subject to compensation when he has been discharged from a job or passed over for promotion. One of the most common errors made by employers is to discharge an employee while he is being treated for a compensable injury. This immediately stirs up resentment to the extent of promoting litigation which might otherwise not materialize.

Aggravation or exaggeration are natural reactions within limits. Oftentimes, the patient feels that some of this is necessary to impress the physician and focus his attention. But, if after good and adequate diagnosis and treatment, this persists to an unusual degree, then watch out for false allegations: (1) Was he ac-

tually injured on the job? (2) Is he responding to treatment? If not, perhaps it would be wise to have consultation or change the treatment, if not the diagnosis.

As to simulation, remember that the attorney and the patient do not have the knowledge and information implicit in *any* physician. Inconsistency of complaints is the earmark of the malingerer.

In closing, I would like to point out a few points of interest: 1. The employer may not appreciate, in fact may actively resent, the conscientious physician in reporting that the condition for which the employee was referred is *not* compensable. This closes the door for employee benefits from the insurance carrier and may place a burden of finance squarely upon the employer in the case of a long-time employee legally or morally entitled to a pension under such circumstances.

2. In denying access to benefits under the Workmen's Compensation Act, the physician must be prepared to reckon with the *union,* and even though he may be 100% in the right, and completely accurate in his evaluation, he may still lose the account from his books.

The industrial physician must always remember that malingering is not compensable, but that conversion reaction (formerly called Hysteria), and always considered by the industrial courts as resulting from the original injury by the nonscientific appellation of *traumatic neurosis,* is fully compensable.

Part III

(Henry J. Climo, M.D.) In discussing the topic of symptom exaggeration, malingering, and conversion reaction from the viewpoints and experience of a physiatrist, and an industrial surgeon alone, one cannot help but be reminded of the old tune "The song is ended but the melody lingers on." In other words, the actual situation, the trauma, which triggered the patient's problem has long since disappeared. Yet, one has the feeling that it is "as if" the trauma is currently present and active. Despite the excellent therapeutic efforts of the physiatrist, the industrial surgeon and others, who in the past have comprised the "medical team," the patient continues to complain. A point is reached where the treating physicians begin to wonder whether or not this patient is a malingerer. His symptoms seem far out of proportion to their objective findings. In fact, the symptoms are almost distorted. It begins to be apparent that the "medical team" treating this patient is lacking something, since the desired results are not forthcoming. As more and more effort is futilely put into the treatment of the patient's now exaggerated symptomatology, the team's attitude becomes almost punitive. Further therapeutic effort expended by the "team" aids in fixing in the patient's mind the feeling that there must be something wrong with him, "because they are continuously testing, examining and treating me." And thus a vicious circle is established until someone rather belatedly, bethinks himself to solicit the aid of the psychiatrist.

The sort of "medical team" commented on is not unlike a two-legged stool unsuccessfully attempting to remain upright. Before giving my view as to why the "medical team," treating such patients must include the psychiatrist, I should first like to depict how this individual, the patient, with his symptom exaggeration came into being.

Fenichel[4] has stated "the basic function of man's mental apparatus following disturbance by any incoming stimuli or excitation whether external or internal, is to re-establish stability in himself." Another word for stability would be equilibrium or homeostasis. This stability, this homeostasis, following the influx of stimuli (excitation) is achieved in the average human being through three modalities: (1) through discharging the stimuli; (2) through binding them and thus rendering them harmless; and (3) through a combination of the two methods.

This influx of stimuli may be so sudden and intense that it will traumatize and disorganize the ego of any individual, the ego being that part of us that sifts and organizes, that discharges and binds, the incoming stimuli and thus renders them harmless. Then again there are incoming stimuli which are harmless for most people but traumatic for certain types of personalities. It is "as if" these latter personalities are "in a state of unconscious readiness" to be traumatically overwhelmed. And it is this latter type of personality that becomes our patients—the subject of this paper. This state of "unconscious readiness" to be overwhelmed involves not only the physical and emotional state of the individual,

but his mobility or passivity at the time the trauma strikes. For example, any soldier would prefer being active, on the move and attacking, to being frozen into inactivity, that is, immobile and "pinned down," in a foxhole by enemy shell-fire. In the latter situation the massive influx of excitation, generated by the awful fear he feels, has no channel or outlet for its dissipation. As a result, a state of emergency within the ego arises, and the ego is now overwhelmed. It is unable to sift and organize, that is discharge and bind, this excitation. The patient is now unable to evaluate appropriately his situation and his actions therefore become purposeless, inadequate, and inappropriate.

Just as plant life trends toward the beneficial effects of sunlight, so does mankind trend toward health, growth and maturity. Thus our patient now finding himself in a state of dysequilibrium, his homeostasis disrupted, tries to reachieve this homeostasis. But with a disintegrated ego this is not quite possible. In our patient's attempts to re-establish this inner stability within himself, he utilizes unsuccessfully his former mature attitudes and actions. Slowly like a retreating army seeking a focus of security, our patient is forced to regress and to resort to infantile, inappropriate and archaic methods. These methods which in early childhood, even infancy, were apparently successful, now do not subserve his purpose. As Freud would have it, this personality has regressed to an immature level.

This is the individual who was sent to you, the physician, for evaluation, complaining bitterly of a somatic complaint. It may be his aching back, his pain in the neck, or any symptom which may be diagnosed "conversion reaction." Although his problem is basically emotional in nature, he comes presenting physical symptoms however, which may be distorted both subjectively and objectively. And however much the treating physician "piles on the treatment," in like manner his symptoms become exaggerated, "heaped up." Why?

Bergler[5] finds, and this finding has been validated by other workers in the field, that many of these patients have an unconscious longing for pain. He calls this longing for pain "psychic-masochism." This would explain "the uncomprehensible" duration of illnesses despite adequate treatment, the relapses and recurrences, the equally illogical and inexplicable attitudes of these patients: such as their failure to follow the doctor's orders, their constant flight from physician to physician, their failure to pay the doctor his just fees, as well as their provocative behavior shown their physician.

Engel,[6] in a brilliant article, feels that many of these individuals utilize pain as a means of subserving unconscious guilt, or of mediating their sado-masochistic drives, and for aggressive and various other purposes.

Brosin[7] states there is a constant interplay between the individual's expression of his personal means, his method of mastering his own drives, his mode of getting satisfaction from these drives, and the culture in which he happens to live at the time. Thus if these individuals stem from an environment in which invalidism and complaining are tolerated, they will naturally resort to this type of response following a severe trauma. Wolff[8] in a brilliant piece of research, similarly concludes that if the patient's culture conditions him to use illness and invalidism to obtain certain satisfactions, commonly called "secondary gains," this is how he will respond in time of stress. Glass[9-11] states that a small minority of patients following danger and disaster will react with disorganized or regressive behavior patterns. It is their inadequate response, to a danger situation that has long since passed, to achieve stability within themselves.

It may be said that whether the trauma is sudden and overwhelming, or whether it affects the patient in small increments over a long period of time, the end result is the same, namely ego disorganization with somatic complaints, which in reality are expressing unresolved emotional conflicts.

The following two brief case histories will illustrate how trauma, in small increments, acting over a long period of time produced the patients' complaints, just as one sees if the trauma to the ego were sudden and overwhelming.

Case 1. Mrs. T. C., a 33 year old white woman, twice married with 3 children from each marriage, a former waitress but now unemployed for over a year, was referred to me by her orthopedist who had been treating her adequately for a pain in the neck of 4 weeks duration.

The following are the events which over a period of time led up to her complaint: With the death of her mother, while still an infant, she of course did not receive the love and attention and affection only a

mother could give. Her siblings and she were dispersed and placed in various relatives' homes, the patient was placed with her sister 10 years her senior. Thus she never knew what it was to "rub elbows" with her siblings. She learned early to sublimate her frustrated drives through a fierce devotion to work, in her job as a waitress. She has worked frequently as many as 20 hours a day, a fact validated by her sister who stated, "She just couldn't say no." Her first marriage ended in tragedy when her husband drowned leaving her with 3 children to support. Her second marriage of 8 years duration is one of constant stress, bickering and fussing about which she does nothing except repress her anger. Increasing obesity following the inordinate intake of food as a substitute for love over the years necessitated her being taken off her feet by her doctor. This added trauma ended her feelings of usefulness. But the doctor did not substitute anything to occupy her idle time, which was spent all day in bed. Thus we see more restlessness, more frustration, more anger but more repression of her feelings.

Comment. Here then we see an ego slowly and continuously traumatized, by increasing stress until 4 weeks prior to being seen by the author, when she developed the pain in the neck. Her symptoms symbolically expressed her feelings about her life situation, namely "a pain in the neck." Adequate treatment by her general practitioner and the referring orthopedist gave some relief but did not remove the cause. Only when the psychiatrist's efforts were added to the medical management did the symptoms begin to abate. For with the basis of her pain in the neck now being treated, in addition to the adequate somatic treatment she received, did beneficial results obtain.

Case 2. J. H., a 36 year old white man, twice married, with 5 children by the second marriage, formerly a building trade worker and now unemployed since December 1956, was referred to me for pain in the lower back of 3 or more years duration (according to the patient).

The following events led up to his complaint of backache: The death of his mother when he was two years of age resulted in the loss of mother's love. The father, a poor farmer, was barely able to give the boy even the most meager necessities of life. He learned to adopt a rather passive attitude toward frustration. This was observed when he married, and later divorced, his first wife, a very immature girl who, he stated "preferred her mama to me." After he left school in the fifth grade he helped a man haul lumber, until his induction into the Army in 1942. In the Army he began "riding the sick book" until finally he received a medical discharge. Interestingly, his job in the Army was simply that of driving a quartermaster truck. After leaving the Army he worked in a textile mill for one year but quit because he could not tolerate indoor work or dust. Actually further probing revealed that he could not tolerate the continuous pressure of his foreman. On Christmas Day 1956, while working at his building trade, under pressure by his boss to finish his job, he "suddenly quit." When he asked his boss for easier jobs the boss said "I do those myself." Thus the patient has not worked since. An iatrogenic factor enters the picture when an examining physician, following x-ray of the patient's spine, purportedly told him that his back bones "were pressed together." Since then he has now begun to feel pain radiating to the nuchal region.

Comment. Therefore in this individual the accumulated stresses acting over a lifetime finally reached their culmination "suddenly on Christmas Day 1956" following which he has been incapacitated. Although he admits that treatment to his back has given him some relief he still lives in the hope that "somewhere, someone, someway, will find something to cure me." Thus he is still trying to reach his state of homeostasis, at the expense of others. How futile would be continued treatment of his back complaint.

Whether our patient is thought to be malingering or showing a conversion reaction, his exaggerated symptomatology is attempting to restore his inner stability. In addition, it is expressing, or masking, unconscious emotional needs. If these needs are, for example, a 10% monthly pension paid by the welfare or Veterans Administration, or extracting the attention, affection and concern from his family, or if guilt or aggressive drives are subserved by his symptom exaggeration, then treating his somatic complaints will not eliminate these needs. His motives are unconscious, therefore he cannot be conscious of the reason for his tenacious complaining. That is, he cannot be aware of the motive that is driving him to do this. For my part therefore, no such condition as malingering exists. I have discovered that, if the so-called malingerer's motives are ferreted out and brought to light, even he becomes no different from the neurotic or other psychiatric casuality.

The conversion reaction type of patient is merely converting the pent-up feeling and tensions which pervades his being that he could not otherwise express, into the form of symptoms, mainly peripheral somatic complaints.[12] But in all these cases these patients are masking a neurotic conflict of long-standing, as well as expressing the need to re-establish their inner stability.

What can be done about this distressful situation—distressful for all concerned? It is my oft-proven opinion that if, at the time the pa-

tient is first evaluated, he also be examined by the psychiatrist, that much chronicity can be mitigated and the patient returned more confidently to his previous state of health. For if you the physiatrist, general practitioner, internist, orthopedist, surgeon, all of you, would permit the psychiatrist to see the patient with you from the beginning, your diagnoses would be harmonized. Then your excellent treatments aided by that which the psychiatrist would offer would bring not only the patient's soma, but his ego to a satisfactory state of health, with homeostasis achieved. Just think what this would mean in terms of monetary savings to the insurance companies which foot the bill? Think also of the savings in your own emotional feelings not to be bedeviled by this "well-meaning, but leech-like" complainer? Thus this troublesome complainer, evaluated and if necessary treated, by all the members of the "medical team," which would include the psychiatrist, would in all probability find his health restored sooner, so that his need for symptom exaggeration, malingering or conversion reaction would be lessened if not eliminated.

In Summary

1. The average individual following trauma can usually be restored to good health following adequate treatment in a reasonable length of time.

2. But the patients who are "unconsciously ready to be overwhelmed and traumatized," in their ego following the best type of treatment even, usually develop symptom exaggeration.

3. These individuals are masking by their complaints their psychiatric problem and are expressing also their need to reach inner stability.

4. Treatment by the medical team as usually constituted without the aid of the psychiatrist may result in a patient with symptom exaggeration.

5. Two brief case histories are cited illustrating the effect of trauma over a long period of time to the ego.

6. The malingerer has been discussed, but even in him, as in other psychiatric casualties, among whom are the patients having conversion hysteria, the motive necessitating his illness is unconscious.

7. It is urged that a psychiatrist be a member of the medical team to evaluate the patient from the very beginning.

8. In this way the chronicity of the illness can be reduced, the tendency to symptom exaggeration mitigated, and the patient restored to homeostasis more quickly.

References

1. Siirde, E. K., Ients, A. K., and Gerassimova, K. V.: (Cited by Fabricant, N.) Vestn. Oto-rino-laring. 1:32, 1957, (The Eye, Ear, Nose & Throat Month. 38:748, 1959.
2. Deyerle, W. M., and May, V. R., Jr.: Sciatic Tension Test, South. M. J. 49:999, 1956.
3. Kirkpatrick, J. E.: Evaluation of Grip Loss, California Med. 85:314, 1956.
4. Fenichel, Otto: The Psychoanalytic Theory of Neurosis. W. W. Norton & Company, Inc., 1946.
5. Bergler, Edmund: Psychiatric Pointers for the General Practitioner, and Internist Treating Psychosomatic Diseases, Dis. Nerv. System 20:420, 1959.
6. Engel, George L.: Psychogenic Pain and the Pain-Prone Patient, Am. J. Med. 26:898, 1959.
7. Brosin, Henry W.: Stress Reactions During Mobilization and Training, Mil. Med. 1:1, 1951.
8. Wolff, Harold G.: Stress, Emotion & Bodily Disease in Civil Life, Mil. Med. 1:34, 1957.
9. Glass, Col. Albert J.: Malingering in Combat Areas, Army Medical Service Graduate School, 1:539, 1952.
10. Glass, Albert J.: Management of Mass Psychiatric Casualties, Mil. Med. 118:335, 1956.
11. Glass, Albert J.: Psychologic Aspects of Disaster, J.A.M.A. 171:222, 1959.
12. Ewalt, J. R., Strecker, E. A., and Ebaugh, F. G.: Practical Clinical Psychiatry. Eighth edition. New York: Blakiston Company (division of McGraw-Hill Book Company, Inc., 1957, pp. 242-246.

Discussion (Abstract)

Dr. Robert Hughes, Atlanta, Ga. Both the malingerer and the conversion hysteria patient report symptoms of somatic illness in situations where such illness serves either as a means of avoiding an unpleasant consequence or of receiving profit. The mechanism and its results are much the same in both cases, except that the patient with the conversion reaction is not conscious of his maneuver and hence actually feels the pain or disability.

My contention is that these two disorders form a continuum with the fully conscious deliberate feigning of illness at one end of the scale and the completely unconscious conversion of anxiety to some organ of the body at the other end of the scale. Implicit in this concept is the idea that the textbook example of either of these conditions is relatively rare and that most cases will fall somewhere between the two extremes. This idea, of course, will explain the difficulty we often experience in diagnosing a specific case as one or the other condition.

Support for this view is found in the fact that the psychotherapeutic approach to the treatment of a conversion reaction consists of first helping the patient to become consciously aware of the protective dynamics of his unconscious mechanism. Typically, when this awareness has been achieved, the patient gives up his symptom and develops an anxiety state which is then treated in the same manner as any other neurotic anxiety.

The determining factor as to where a given case will fall on the scale is the strength of the patient's conscience. At the one extreme we find the psycopath who

is lacking in conscience and at the other extreme we find the neurotic whose conscience is so strong that it dominates his life. Between these two extremes we find the person with psycopathic tendencies with an almost conscious awareness of what is going on and the person with neurotic tendencies who may be able to admit to himself that the illness, although real, does benefit him.

ARE YOU MOVING?

Please send the following to: Southern Medical Association

2601 Highland Avenue, Birmingham 5, Alabama

Name.....
(Please print)

Old Address:	New Address:
Street.....	Street.....
City and Zone.....	City and Zone.....
State.....	State.....

The Late Stage of the Myeloproliferative Syndrome: Case Reports

JOHN V. DENKO, M.D.,† *Amarillo, Tex.*

THE CLINICAL PICTURE of the myeloproliferative syndrome is variable and depends on the phase when the disease is recognized. The most frequent complaints the patients have are fatigue, weakness, weight loss and pressure symptoms of an enlarged spleen. Signs of hepatic involvement with hemorrhagic tendencies, ascites and ankle edema may also be present.

Peripheral blood studies present the first definite clue with evidence of a fairly severe normochromic or macrocytic anemia with a few immature granulocytes and frequently increased abnormal platelets. When the peripheral leukocyte count is elevated the picture may be similar to chronic myelocytic leukemia. If the leukocyte count is low there is less of a leukemoid reaction.

Bone marrow aspirations are usually dry or hypocellular in the late stage of the disease[1,2] and a biopsy is needed to evaluate the state of the marrow. The biopsy will frequently show spicules of proliferative bone in the marrow portions, and much of the fatty and hematopoietic substance is replaced with fibrous tissue containing scattered hematopoietic cells. The hematopoietic cells frequently show increased myelocytic forms[12] and increased abnormal megakaryocytes. Occasionally hyperplastic marrow has been reported. Needle biopsy of the spleen will show myeloid metaplasia and a similar finding may be present in the liver to a lesser degree.[3]

Since 1879, when Heuck[4] reported the first clinical case of myelofibrosis much has been written and said about the etiology, diagnosis and treatment of this syndrome. Much of the early literature is confusing and many descriptive terms have been applied to the syndrome. These include agnogenic myeloid metaplasia, pseudoleukemia, myeloid metaplasia, leukoerythroblastosis, chronic nonleukemic myelosis, hepatosplenomegaly, aleukemic myelosis, erythroblastosis and a dozen other names.[11]

In 1950, Wyatt and Sommers[2] found 129 acceptable cases in the literature and added 30 more. The myeloproliferative syndrome has been reported with more frequency in recent years.

This report deals with 4 patients having myeloproliferative syndrome; one patient presented evidence of portal hypertension that was measured at operation, at which time esophageal, gastric and splenic varices were found.

In reference to the portal sinusoidal obstruction of venous flow, Wyatt and Sommers[2] reported 3 patients out of 30 who had gastric and esophageal varices. In other series no reference is made to varices although in a high percentage of cases there developed ascites, hematemesis and occasionally tarry stools, and frequently symptoms of right heart failure.[1,5-7]

Case Reports

Case 1. This 48 year old man was first seen in 1950 when he suffered a bout of hematemesis and had tarry stools. The physical examination disclosed no enlargement of the liver or spleen. His Hgb. was 8.1 Gm.,—the RBC. 2.8 million and the WBC. 5,900 per cu. mm. Liver function tests were normal. The roentgenograms of the upper gastrointestinal tract showed no abnormalities. The patient gave a past history of acute alcoholism for one week before admission.

He was seen again in 1951 (17 months later) with complaints on admission of dyspnea, weakness, diarrhea and swelling of his abdomen and ankles for two weeks. When in Japan 8 months before he had a possible history of infectious hepatitis. On this admission

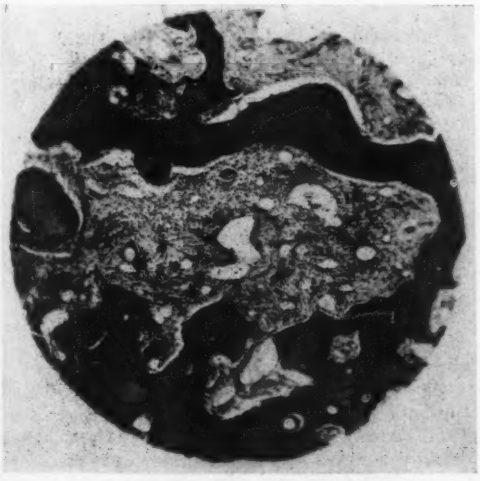
†From the Department of Pathology, Northwest Texas Hospital, Amarillo, Tex.

there was ascites, and both the liver and spleen were enlarged and nontender. Laboratory studies showed a severe normochromic anemia with a Hgb. of 5.3 Gm., and a RBC. of 1.78 million.[8] The WBC. was 13,700, with 37% lymphocytes and 57% neutrophils with a leukemoid reaction. Thymol turbidity and cephalin flocculation tests were normal. Serum proteins were 5.9 Gm. with 4.2 Gm. of albumin and 1.7 Gm. globulin per 100 cc. Urinalysis was normal. Saline fragility of erythrocytes was normal. Reticulocyte count was 2.8 per cent. The Coombs test was positive. Several marrow aspirations were attempted to evaluate further his anemia, and several attempts at different sites were unsuccessful. He received supportive transfusions, diuretics, vitamin K, choline and antibiotics. He was discharged with a diagnosis of cirrhosis of the liver with esophageal varices and gastroenteritis.

The patient was admitted for the third time 8 months later in 1952. He complained of weakness and fatigue. He also gave a history of alcoholic intake since his last admission. On physical examination the head, neck and chest were not remarkable. The liver edge was 8 cm. below the right costal margin and a massive firm spleen filled the left side of the abdomen. Laboratory studies showed a Hgb. of 8.4 Gm., with 3.2 million erythrocytes, and a leukocyte count of 3,350 cells per cu. mm. with a shift to the left. Erythrocytes showed anisocytosis. Bromsulphalein retention was 6% at 45 min. Cephalin flocculation was 4+; serum bilirubin was 1.2 mg. per 100 cc.; prothrombin time was 65% of normal. The thymol turbidity was normal. Bone marrow biopsy was done and extensive myelofibrosis and sclerosis were found (Fig. 1).

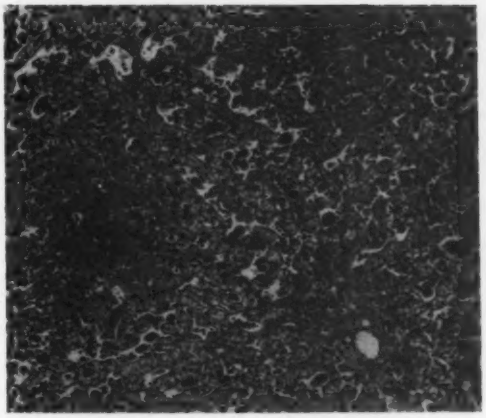
Since a diagnosis of esophageal varices and hepatic cirrhosis had been made previously and a Banti-like picture was present, a portacaval shunt operation was performed. The portal vein pressure was 320 mm. of water (normal 85 to 150 mm.). The operation was successfully completed. After operation the pressure

FIG. 1



(Case 1) Osteosclerosis and myelofibrosis.

FIG. 2



(Case 1) Liver with intrasinusoidal hematopoiesis. (x80 H & E)

dropped to 220 mm. A liver biopsy taken at the time of operation disclosed extensive hematopoiesis (Fig. 2). Special hematologic studies done after operation disclosed an iron turnover of 61.9 mg. daily. The Ashby survival time was normal and there was reported no splenic destruction of erythrocytes. The serum iron was 47 gamma per 100 cc. The patient was discharged markedly improved with an erythrocyte count of 4 million, normal serum bilirubin, cephalin flocculation and serum proteins.

The patient's last admission was 2 months later. He was admitted with complaints of a cough, chest pain, dyspnea, fever and weakness. On physical examination an enlarged liver and massive spleen were palpable. Chest roentgenogram disclosed an organizing pneumonitis. The erythrocyte count was 2.2 million and Hgb. was 5.7 Gm. WBC. was 3,100 cells with a shift to the left. The sedimentation rate was 123 mm. per 1 hour. Alkaline phosphatase was 18.6 Bodansky units. The other liver function tests repeated were normal.

The patient received transfusions and supportive therapy. He was improved at intervals and utilized 19 units of blood in 5 months. He became lethargic and expired 5 months after admission, approximately 3 years after his first symptoms.

Autopsy Findings: Only pertinent findings are mentioned. The site of the portacaval shunt operation was intact and adequately patent. Massive dilated veins were present over the dome of the diaphragm with marked dilatation of the splenic, gastric and esophageal veins. The liver weighed 3,500 Gm. The parenchyma was firm and reddish-mahogany brown. Microscopic section (Fig. 2) disclosed pronounced extramedullary hematopoiesis in the sinusoids. The spleen weighed 2,350 Gm. and on cut surface it was firm and had a reddish-tan color of liver parenchyma. Histologic sections disclosed extensive extramedullary hematopoiesis with myeloid, erythroid cells and megakaryocytes. Hemosiderin was abundant. The lungs showed lobar pneumonia in both lower lobes. Adrenals, thyroid, kidneys, and testes all showed some small foci of

infiltration of metamyelocytes microscopically. Lymph nodes were enlarged, soft and gray-tan. Microscopically they showed extramedullary hematopoiesis. Bone marrow from the sternum, rib, vertebrae and iliac crest all showed a dense whitish bone tissue that microscopically disclosed myelosclerosis with marrow proliferations of abnormal megakaryocytes with foci of hematopoietic cells (Fig. 1).

Case 2. On admission to the hospital this 70 year old white man complained of weakness, fatigue, nausea and malaise. Two years before he received some radiation therapy for pressure symptoms from an enlarged spleen. After 2 weeks of therapy he discontinued the treatments since he felt no better. He was reasonably well until 2 days before admission. His past history was non-contributory. He had been in good health except for a bout of "asthma" 4 years before.

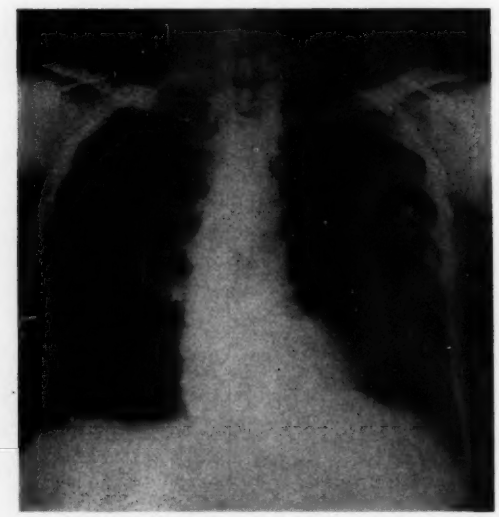
Physical examination disclosed a chronically ill appearing man with a normal pulse, respiration and temperature. Examination of the head, neck and chest was not unusual. The abdomen was protuberant with a large, hard, nontender spleen. The liver was not palpable.

Laboratory studies showed a Hgb. of 9.1 Gm., the PCV. 30 vol. %; the WBC. was 30,300 with 20% lymphocytes, 58% neutrophils and 22% myelocytes. The bleeding and clotting times were normal; alkaline phosphatase, thymol turbidity and cephalin flocculation were normal. Roentgenogram of the chest disclosed increased density of the trabeculations (Fig. 3). Bone marrow aspirations on two attempts were not satisfactory due to poor cellularity which showed a relative increase in myeloid cells.

The clinical impression was chronic myeloid leukemia. The patient expired 3 weeks after admission with temperature 104°, lethargy and confusion.

Autopsy Findings (Pertinent findings): The enlarged spleen weighed 2,450 Gm. and microscopically had prominent myeloid, erythroid, and megakaryocytic cells. There was excessive stromal collagen proliferation about the trabeculae in the spleen obliterating the follicles. The liver was 2,700 Gm. with a smooth capsule and pale tan parenchyma with small foci of extramedullary hematopoiesis in sinusoids. Lymph nodes were enlarged, firm and gray-tan; microscopically myeloid, erythroid and megakaryocytic cells were present. There was some excessive fibrosis of the stroma. Bone marrow from the ribs, vertebrae and iliac crest was pale and fibrotic. Microsections disclosed a diffuse proliferation of fibrous and bony tissue in the marrow with scattered isolated hematopoietic cells of the myeloid series with only a few erythroid cells and megakaryocytes and many bizarre platelets. In the gastrointestinal tract no esophageal or gastric varices were noted.

FIG. 3



(Case 2) Roentgenogram shows abnormal increased fine trabeculation of the bone.

Case 3. This 76 year old white man was admitted to the hospital with complaints of weakness, malaise and weight loss. His temperature, pulse and respirations were normal.

Physical examination showed head and neck to be normal. The roentgenogram of the chest was normal also. The liver was not palpable but the spleen was markedly enlarged, firm and nontender. There was no lymph adenopathy. The gastrointestinal roentgenograms were negative.

Laboratory studies revealed a RBC. of 3,020,000 and WBC. of 7,000 per cu. mm. Hgb. was 9.6 Gm. The erythrocytes showed moderate anisocytosis and poikilocytosis. The differential count showed a leukemoid reaction with a few myelocytes and 15% metamyelocytes. Occasional nucleated red cells were also found. Liver function studies were normal. Biopsy of bone marrow from both the sternum and iliac crest showed prominent myelofibrosis of bone.

Course: The patient received blood transfusions and was discharged. He was given periodic transfusions for recurrent anemia and was treated with steroids. On Dec. 20, 1957, the patient expired at home following a massive hematemesis, two and one-half years after diagnosis. No autopsy was obtained.

Case 4. This 48 year old woman was first admitted to the hospital in August 1957, with complaints of weakness, malaise, fatigue and weight loss for 4 months. On physical examination nothing unusual was reported. The RBC. was 3,520,000 and the WBC. 3,000 cells per cu. mm., with a normal differential white count. The sedimentation rate was 141 mm. per 1 hour (Westergren). The urine contained a trace of protein. After transfusions the patient was discharged without a diagnosis.

The patient's second admission was 3 months later in November, when she complained of weakness and fatigue. On physical examination the liver and spleen were noted to be easily palpable and nontender. There was no ascites or edema. The gastrointestinal series and chest roentgenograms were normal. Roentgenograms showed no abnormalities of the bones.

The laboratory studies disclosed a Hgb. of 8.7 Gm., RBC. of 3,120,000 and WBC. of 3,850 cells per cu. mm. The differential white count revealed 13 stab forms; excessive numbers of platelets were noted. The platelet count was 325,500. The urinalysis was normal.

Liver function tests showed a cephalin flocculation of 4+, alkaline phosphatase of 17.8 Bodansky units, serum bilirubin of 1.6 mg. per 100 cc. The serum proteins were 7.14 Gm. with 2.7 Gm. albumin and 4.42 Gm. of globulin per 100 cc. Prothrombin time was 14 sec. Febrile agglutinations were negative. L. E. cell studies were negative. Biopsy of the bone marrow disclosed an extensive myelofibrosis with early osteosclerosis. A needle biopsy of the liver showed extensive fatty metamorphosis and no evidence of extramedullary hematopoiesis. The patient received transfusion and was placed on steroid therapy before being discharged.

Her third admission was about one month later, on January 10, with a severe herpes zoster of her chest. She had felt some subjective improvement while on prednisone (Meticorten) and antibiotics continually. She was admitted for transfusions. The peripheral blood continued to show a leukemoid picture.

The patient's fourth admission was January 26, when she developed chills and a fever of 103°. On this admission it was learned that the patient's sister, brother and mother all had died of leukemia. Laboratory studies showed a Hgb. of 9 Gm., a RBC. of 3.6 million and a WBC. of 2,600 per cu. mm. On differential white count 9 lymphocytes, 81 segmented neutrophils and 10 stab forms were found. Serum bilirubin was 4.4 mg. per 100 cc. The alkaline phosphatase was 23.6 Bodansky units. The urine contained +2 albumin. Roentgenograms of the chest disclosed a patchy consolidation in the upper lobes of both lungs.

The patient's temperature fluctuated from normal to 103° daily. She developed ecchymoses of the skin over her chest. After blood transfusions she was discharged at her insistence.

Her last admission was on Feb. 4, 1958, with an episode of rectal bleeding and continued weakness and fever. The liver and spleen remained enlarged. She developed large ecchymoses over her entire body as well as icterus. She became progressively weaker and expired.

Autopsy Findings: (Only the pertinent findings are reported.) The lungs had foci of small infarcts with many small foci of necrosis and monilia proliferating in the necrotic parenchyma. The spleen weighed 750 Gm. The cut surface was firm, meaty red with no recognizable follicles. Microscopically there was a diffuse hematopoiesis present with erythroid, myeloid cells and megakaryocytes. There was also an increase in collagenous stroma proliferation about the trabeculae. Hemosiderin deposition was abundant. The gastrointestinal tract showed an ulceration present in the lower part of the esophagus but no varices were present. The liver weighed 2,300 Gm.; it was pale yellow with some dark hemorrhagic areas. Histologic sections disclosed a severe fatty metamorphosis of the cells with extensive vacuolization. There were small scattered foci of extramedullary hematopoiesis as well as stromal fibrosis and atrophy of liver cells suggestive of the splenic fibrous proliferation. The hematopoiesis was only patchy and not extensive. There were several large areas of necrosis with hemorrhage in the liver parenchyma.

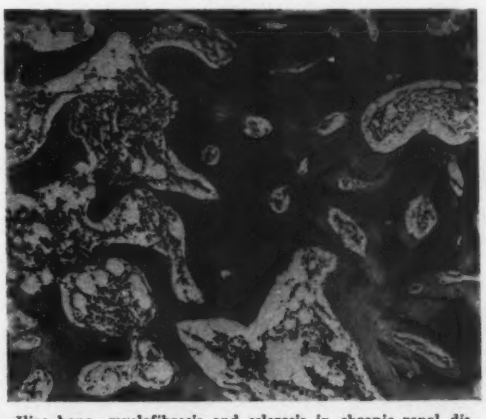
Lymph nodes were enlarged, firm and pale. Histologically, areas of fibrosis and hematopoieses were found. In the stroma of the kidney a few foci of hematopoiesis were found. Bone marrow was grossly dark, gray-brown and firm. Histologically, there was dense fibrosis of the marrow with remnants of hematopoietic cells of the erythroid, myeloid series and many bizarre megakaryocytes.

Comment on Cases Presented. All the patients presented had myelofibrosis of varying degree. All initially gave symptoms referable to anemia and splenic enlargement. The laboratory findings were similar, showing a leukemoid picture, although the white count varied from 3,000 to 30,000. Liver function tests in cases 1 and 4 presented evidence of parenchymal damage which had persisted in case 4 until postmortem examination. Case 1 had been initially confused with cirrhosis of the liver since esophageal varices and portal hypertension were demonstrated. Case 3 was confused with chronic myeloid leukemia. The patients in cases 2 and 4 were diagnosed and treated for myelofibrosis and myeloid metaplasia without much success. Patients 1 and 4 died from lung infections. Roentgenogram evidence of osteosclerosis was reported on Case 3 and has been well documented in other series.[5,9] The bone sclerosis present differs considerably from other forms of osteosclerosis such as that found associated in chronic renal disease.[10] The reticuloendothelial system does not show the abnormal proliferation (Fig. 4).

Discussion

Myelofibrosis and myeloid metaplasia are regarded as a mesenchymal reaction to injury. It should also be emphasized that the spleen

FIG. 4



Iliac bone—myelofibrosis and sclerosis in chronic renal disease (x 63 H & E).

and lymph nodes may develop stromal fibrosis as well as the myeloid metaplasia. This was evident in cases 2 and 4. Peace[1] and Wyatt and Sommers[2] utilize the term myelonecrosis as the primary lesion followed with the late stage of myelosclerosis.

Variable agents have been incriminated as causing myelosclerosis and chronic marrow failure. These include extrinsic toxic agents as, for example, benzene and radioactive material. Other agents incriminated are related to endocrine disease and liver dysfunction. Wyatt and Sommers[2] believe liver dysfunction is one of the main possible causes of chronic marrow failure and myelosclerosis. They state that benzene and related aromatic compounds are known to be metabolized by oxidation to phenol, catechol and hydroquinone, which are normally rapidly conjugated in the liver to sulfates and glucuronates which are excreted. Adrenal cortical and estrogenic steroids which possess phenolic or quinone groups are similarly conjugated and excreted by the liver. Failure of efficient hepatic conjugation exposes the tissues to higher concentrations of these substances which are toxic to hematopoietic cells. There is experimental evidence that nucleoproteins have a myelostimulatory action and can induce proliferation of immature hematopoietic cells in the marrow and undifferentiated mesenchyme of the remaining reticuloendothelium system.

Summary

1. Four cases of myelofibrosis with myeloid metaplasia are presented. Three are cases with autopsy reports and one with marrow biopsies.

2. One case presented morphologic and clinical physiologic evidence of portal hypertension due to the extramedullary hematopoiesis in the sinusoids producing partial obstruction to portal flow. Venous pressures measured are the first reported in the literature in a patient with hematopoiesis of the liver due to myelosclerosis.

3. The osteosclerosis that develops differs considerably from osteosclerosis in other disorders like chronic renal disease which shows no abnormal marrow proliferations.

4. The findings of abnormal liver function tests in two cases support the theory of Wyatt and Sommers that parenchymal liver damage may be the initiating factor in the production of endogenous products of metabolism which are cytotoxic agents, responsible for the injury to the reticuloendothelial system with secondary myelostimulatory response of extramedullary hematopoiesis, whose reparative process ends as a myelosclerosis in the marrow.

References

1. Peace, Robert J.: Myelonecrosis, Extramedullary Myelopoiesis, and Leukoerythroblastosis, Am. J. of Path. 29: 1029, 1953.
2. Wyatt, John P., and Sommers, Sheldon C.: Chronic Marrow Failure, Myelosclerosis and Extramedullary Hematopoiesis, Blood 5:329, 1950.
3. Block, Matthew, and Jacobson, Leon O.: Myeloid Metaplasia, J.A.M.A. 143:1390, 1950.
4. Heuck, G.: Zwei Falle von Leukaemie mit eigenthun Lichen Blut-resp. Knochenmarks Befund, Virchows Arch. path. Anat. 78:475, 1879.
5. Hickling, R. A.: Chronic Non-Leukemic Myelosis, Quart. J. Med. 6:253, 1937.
6. Hutt, M. S. R., Pinniger, D. M., and Wetherley-Mein, G.: The Myeloproliferative Disorders with Special Reference to Myelofibrosis, Blood 8:295, 1953.
7. Jackson, H., Jr., Parker, F., Jr., and Lemmon, H. M.: Agnogenic Myeloid Metaplasia of the Spleen, New England J. Med. 222:985, 1940.
8. Green, T. W., Conley, C. L., Ashburn, L. L., and Peters, H. R.: Splenectomy for Myeloid Metaplasia of the Spleen, New England J. Med. 248:211, 1953.
9. Richmond, John, and Duncan, J. G.: Myelofibrosis and Myelosclerosis, Scottish Med. J. 1:357, 1956.
10. Wolf, Horace L., and Denko, John V.: Osteosclerosis in Chronic Renal Disease, Am. J. M. Sc. 235:33, 1958.
11. Cook, J. E., Franklin, J. W., Hamilton, H. E., and Fowler, W. M.: The Syndrome of Myelofibrosis, A.M.A. Arch. Int. Med. 91:704, 1953.
12. Wiltshaw, E., and Moloney, W. C.: Histochemical and Biochemical Studies on Leukocyte Alkaline Phosphatase Activity, Blood 10:1120, 1955.

A man in good health is always full of advice to the sick.
—Menander

The New Obstetric Patient*

GEORGE S. ALLEN, M.D., *Louisville, Ky.*

THE DOCTORS OF THIS AUDIENCE deliver quite an addition to the Nation's population each year. My topic is the very broad one of the new obstetric patient. Perhaps a reasonable beginning would be a consideration of just who the new obstetric patient might be. Primarily, she is pregnant. Most of the time such a patient presents herself with a remark such as "I want to see if I am pregnant." Our initial approach therefore is a diagnostic one. Usually pelvic examination alone reveals the answer, particularly if she has missed the second period. Occasionally, however, the patient may be extremely anxious either to be pregnant, or not to be, and may come to us because she is only a few days past her expected menstrual period. In such cases, of course, we resort to pregnancy testing to arrive at an accurate diagnosis.

Once the diagnosis of pregnancy is established, we have a new obstetric patient; usually she is in the final stages of the first trimester. She may, of course, be either a primigravida or a multipara, but in either case she has come to us after some deliberation. Many new patients are referred by other patients or other physicians. Some come because we are convenient to their homes or their neighborhood, and they have heard that we do obstetric work. The doctor's individual reputation in some way usually has played a major role in the patient's selection. The occasion of her first prenatal visit, therefore, is a highly important one to the successful management of her entire pregnancy.

The new obstetric patient subjects us, our offices, and our assistants to the same kind of a scrutiny we give a new house and real estate company if we happen to be in that market. This patient has heard about us, she is now checking on what she has heard. In addition, this patient has a certain background of information, or very frequently misinformation, about pregnancy and childbirth. Of course she has read the papers and the magazines, has heard about hypnotism, knows about cesarean section, and has heard about doctors starting labor. She knows something about twilight sleep and usually wants to know a little bit more about it. In all, this patient has been schooled by the sum total of obstetric information that emanates from family, lay press, and social gatherings. If our new obstetric patient happens to be a primigravida, she frequently has an Aunt Maud or a reasonable counterpart who has been enlightening her about pregnancy by recounting her experience. I am sure you will all recognize the story in some one of its many forms—the aunt or relative who says to our new pregnant patient, "My God, honey, I hope you don't have the kind of time I had with cousin Charles. Why, I laid in labor for 4 days, and then they had to take the baby with instruments." Now this type of old wives' tales and this information, I am certain all of you realize, can color the attitude and approach to pregnancy of our new patient—and such a colored attitude from our point of view, certainly is something short of spectacular.

Our patient may be a multipara and such a new patient logically should raise in our mind the question "why"? Why is this patient—a multipara—coming to us at this time? Immediately we recognize many reasons why a multipara might change doctors. Some of them are the subject of jokes among us. There is almost an axion—beware of the new multipara who comes in complaining about her previous physician. Check with the doctor that delivered her previously and see if the bill has been paid. Naturally, all of us recognize and contend with patients who skip from doctor to doctor leaving a trail of unpaid medical accounts. These patients, however, are not a majority. Patients also change doctors for other reasons. Many of them are new arrivals to our city or our neighborhood, and it is inexpedient for them to return to the physician who delivered them previously. I believe our consideration this evening should be with the multiparous patient who has been delivered previously by a colleague, and who for some

*Read before the Section on General Practice, Southern Medical Association, Fifty-Third Annual Meeting, Atlanta, Ga., November 16-19, 1959.

and lymph nodes may develop stromal fibrosis as well as the myeloid metaplasia. This was evident in cases 2 and 4. Peace[1] and Wyatt and Sommers[2] utilize the term myelonecrosis as the primary lesion followed with the late stage of myelosclerosis.

Variable agents have been incriminated as causing myelosclerosis and chronic marrow failure. These include extrinsic toxic agents as, for example, benzene and radioactive material. Other agents incriminated are related to endocrine disease and liver dysfunction. Wyatt and Sommers[2] believe liver dysfunction is one of the main possible causes of chronic marrow failure and myelosclerosis. They state that benzene and related aromatic compounds are known to be metabolized by oxidation to phenol, catechol and hydroquinone, which are normally rapidly conjugated in the liver to sulfates and glucuronates which are excreted. Adrenal cortical and estrogenic steroids which possess phenolic or quinone groups are similarly conjugated and excreted by the liver. Failure of efficient hepatic conjugation exposes the tissues to higher concentrations of these substances which are toxic to hematopoietic cells. There is experimental evidence that nucleoproteins have a myelostimulatory action and can induce proliferation of immature hematopoietic cells in the marrow and undifferentiated mesenchyme of the remaining reticuloendothelium system.

Summary

1. Four cases of myelofibrosis with myeloid metaplasia are presented. Three are cases with autopsy reports and one with marrow biopsies.

2. One case presented morphologic and clinical physiologic evidence of portal hypertension due to the extramedullary hematopoiesis in the sinusoids producing partial obstruction to portal flow. Venous pressures measured are the first reported in the literature in a patient with hematopoiesis of the liver due to myelosclerosis.

3. The osteosclerosis that develops differs considerably from osteosclerosis in other disorders like chronic renal disease which shows no abnormal marrow proliferations.

4. The findings of abnormal liver function tests in two cases support the theory of Wyatt and Sommers that parenchymal liver damage may be the initiating factor in the production of endogenous products of metabolism which are cytotoxic agents, responsible for the injury to the reticuloendothelial system with secondary myelostimulatory response of extramedullary hematopoiesis, whose reparative process ends as a myelosclerosis in the marrow.

References

1. Peace, Robert J.: Myelonecrosis, Extramedullary Myelopoiesis, and Leukoerythroblastosis, Am. J. of Path. 29: 1029, 1953.
2. Wyatt, John P., and Sommers, Sheldon C.: Chronic Marrow Failure, Myelosclerosis and Extramedullary Hematopoiesis, Blood 5:329, 1950.
3. Block, Matthew, and Jacobson, Leon O.: Myeloid Metaplasia, J.A.M.A. 143:1390, 1950.
4. Heuck, G.: Zwei Falle von Leukaemie mit eigenthun Lichen Blut-resp. Knochenmarks Befund, Virchows Arch. path. Anat. 78:475, 1879.
5. Hickling, R. A.: Chronic Non-Leukemic Myelosis, Quart. J. Med. 6:253, 1937.
6. Hutt, M. S. R., Pinniger, D. M., and Wetherley-Mein, G.: The Myeloproliferative Disorders with Special Reference to Myelofibrosis, Blood 8:295, 1953.
7. Jackson, H., Jr., Parker, F., Jr., and Lemmon, H. M.: Agnogenic Myeloid Metaplasia of the Spleen, New England J. Med. 222:985, 1940.
8. Green, T. W., Conley, C. L., Ashburn, L. L., and Peters, H. R.: Splenectomy for Myeloid Metaplasia of the Spleen, New England J. Med. 248:211, 1953.
9. Richmond, John, and Duncan, J. G.: Myelofibrosis and Myelosclerosis, Scottish Med. J. 1:337, 1956.
10. Wolf, Horace L., and Denko, John V.: Osteosclerosis in Chronic Renal Disease, Am. J. M. Sc. 235:33, 1958.
11. Cook, J. E., Franklin, J. W., Hamilton, H. E., and Fowler, W. M.: The Syndrome of Myelofibrosis, A.M.A. Arch. Int. Med. 91:704, 1953.
12. Wiltshaw, E., and Moloney, W. C.: Histochemical and Biochemical Studies on Leukocyte Alkaline Phosphatase Activity, Blood 10:1120, 1955.

A man in good health is always full of advice to the sick.
—Menander

The New Obstetric Patient*

GEORGE S. ALLEN, M.D., *Louisville, Ky.*

THE DOCTORS OF THIS AUDIENCE deliver quite an addition to the Nation's population each year. My topic is the very broad one of the new obstetric patient. Perhaps a reasonable beginning would be a consideration of just who the new obstetric patient might be. Primarily, she is pregnant. Most of the time such a patient presents herself with a remark such as "I want to see if I am pregnant." Our initial approach therefore is a diagnostic one. Usually pelvic examination alone reveals the answer, particularly if she has missed the second period. Occasionally, however, the patient may be extremely anxious either to be pregnant, or not to be, and may come to us because she is only a few days past her expected menstrual period. In such cases, of course, we resort to pregnancy testing to arrive at an accurate diagnosis.

Once the diagnosis of pregnancy is established, we have a new obstetric patient; usually she is in the final stages of the first trimester. She may, of course, be either a primigravida or a multipara, but in either case she has come to us after some deliberation. Many new patients are referred by other patients or other physicians. Some come because we are convenient to their homes or their neighborhood, and they have heard that we do obstetric work. The doctor's individual reputation in some way usually has played a major role in the patient's selection. The occasion of her first prenatal visit, therefore, is a highly important one to the successful management of her entire pregnancy.

The new obstetric patient subjects us, our offices, and our assistants to the same kind of a scrutiny we give a new house and real estate company if we happen to be in that market. This patient has heard about us, she is now checking on what she has heard. In addition, this patient has a certain background of information, or very frequently misinformation, about pregnancy and childbirth. Of course she has read the papers and the magazines, has heard about hypnotism, knows about cesarean section, and has heard about doctors starting labor. She knows something about twilight sleep and usually wants to know a little bit more about it. In all, this patient has been schooled by the sum total of obstetric information that emanates from family, lay press, and social gatherings. If our new obstetric patient happens to be a primigravida, she frequently has an Aunt Maud or a reasonable counterpart who has been enlightening her about pregnancy by recounting her experience. I am sure you will all recognize the story in some one of its many forms—the aunt or relative who says to our new pregnant patient, "My God, honey, I hope you don't have the kind of time I had with cousin Charles. Why, I laid in labor for 4 days, and then they had to take the baby with instruments." Now this type of old wives' tales and this information, I am certain all of you realize, can color the attitude and approach to pregnancy of our new patient—and such a colored attitude from our point of view, certainly is something short of spectacular.

Our patient may be a multipara and such a new patient logically should raise in our mind the question "why"? Why is this patient—a multipara—coming to us at this time? Immediately we recognize many reasons why a multipara might change doctors. Some of them are the subject of jokes among us. There is almost an axion—beware of the new multipara who comes in complaining about her previous physician. Check with the doctor that delivered her previously and see if the bill has been paid. Naturally, all of us recognize and contend with patients who skip from doctor to doctor leaving a trail of unpaid medical accounts. These patients, however, are not a majority. Patients also change doctors for other reasons. Many of them are new arrivals to our city or our neighborhood, and it is inexpedient for them to return to the physician who delivered them previously. I believe our consideration this evening should be with the multiparous patient who has been delivered previously by a colleague, and who for some

*Read before the Section on General Practice, Southern Medical Association, Fifty-Third Annual Meeting, Atlanta, Ga., November 16-19, 1959.

reason, known best to her, has seen fit to change doctors.

The technic of antenatal care is fairly standardized from the physical point of view. As medical students we are taught what good obstetric care should include. We realize that every new obstetric patient is entitled to a thorough physical examination, and an evaluation of her past medical and obstetric history and an accurate menstrual history—all of these procedures are more or less taken for granted as being representative of good prenatal care. Naturally, we do the necessary laboratory studies—evaluation of the state of the hemoglobin and hematocrit, an urinalysis, and RH typing. These are standard among all physicians.

The variables of prenatal care actually are two—these variables are the patient and the physician. Probably it is safe to assume that in at least 50% of the instances in which a new obstetric patient is a multipara who has been delivered previously by one of our colleagues, the doctor-patient relationship was not satisfactory—at least from her point of view, and very possibly not satisfactory from his. The rapport or doctor-patient relationship that must exist in every obstetric case is a subject that needs our sober consideration, and probably explains much of the difference between the obstetric care of one doctor as compared to another. This doctor-patient relationship in obstetrics is all important, and cannot be a constant thing since it depends upon two variables, the physician and the patient. It is necessary, however, that it be established in a satisfactory manner in terms of the personalities of these two individuals. This relationship is the rapport that doctors strive to establish. If it were simple to establish, and if it were constantly maintained, there would be no changing of doctor by patients. Rapport begins at the first prenatal visit, and if it is not established then the chances of establishing it in subsequent visits are rather slim. Rapport is necessary to afford the patient proper instruction and management. Actually, when it is present it is truly strengthened by instruction. Rapport is confidence; rapport is friendship; it is a patient liking her doctor, and a doctor liking his patient. Rapport is also respect, mutually granted between the two individuals. All of these things may be present between a doctor and his patient, and yet to an observer rapport between one doctor and his patient may appear quite different than the rapport between another doctor and another patient. Certainly, rapport is not a scientific thing. It is the *sine quo non* of the art of medicine, and in my opinion, tends to be more necessary, more valuable, and more strengthened in obstetrics than in any other phase of medicine.

Our new patient's first visit, therefore, offers the opportunity to establish rapport. She has gone more than halfway in this regard by the very fact that she comes to us. Consequently, the burden of proof is upon us. We must realize that we are individuals; perhaps we must examine our own attitudes about the work we do. Perhaps we should ask ourselves how we really feel about pregnancy—what we really think about labor! These things are important, because in some measure there is bound to be a transference of our attitudes to the patient. I do not propose to outline a *modus operandi* for the first prenatal visit. It is rather like the Viceroy ad—to each his own. There are certain broad principles, however, that are fairly universally accepted. The patients do not wish to be rushed. Certainly this is true at the initial visit. Patients appreciate thoroughness. The complaint we hear so frequently, of the rapid examination, is not new. The patient does not appreciate this type of insinuation; she does not like feeling as though she is a gnat on the end of your nose. Patients do not wish to be looked down upon, or to be talked down to. There is enough intrinsic mystery in childbirth without a physician mystifying his patient by his procedures. Finally, I think we might all do well to recall the advice given so frequently by the late Dr. John Walker Moore. I am sure many of you will remember his admonition to the medical students to listen to the patients and they will tell you what is wrong with them. If on the occasion of the first prenatal visit, the patient is received warmly and with understanding, and if the diagnostic and examining procedures are explained to her at the time, almost invariably the patient will accept us, and the first step in the establishment of good rapport will have been taken. After all, as I stated previously, the patient has gone more than halfway. She is actually asking for the establishment of rapport by the very fact that she has selected us to deliver her child.

Once the rapport is established, in my opin-

ion it becomes the task of the physician to instruct the patient about childbirth and about pregnancy, and about labor in honest terms. The greatest enemy to good obstetric care is fear. Fear is the product of ignorance, and the antidote for ignorance is instruction. It is my firm belief, and I am reasonably certain that your own experience will bear this out, that the well-integrated patient—the patient who knows fairly well what to expect of pregnancy, labor, and of birth—usually has a labor that is not awesome to behold—rather it is a pleasant experience to observe. The patient who knows the score obstetrically, so to speak, is not likely to climb the wall. Her requirement of sedation will be certainly less than the tense and apprehensive patient. I believe that tenseness and apprehension can in large measure be drastically reduced by instruction of the patient in the prenatal period. Now the method of instruction will naturally vary from physician to physician.

Personally, I have been quite interested in a group method and have found it quite satisfactory.[1] It seems to me that the group type of antenatal care is well adapted to the Family Doctor. First of all, there is a natural feeling of sorority among gravid women—invariably they smile at one another. This natural affinity can become a valuable antenatal aid in the classroom approach. In my own experience, I have found informality to be the keynote of effectiveness. We have used a general outline and employ a series of specially designed movies. These movies set a theme of discussion which follows later. The patients are grouped according to E.C.D., and after the first session a remarkable *esprit de corps* develops. The women become highly interested in pregnancy —both their own and that of their classmates. In this way and through honest friendly instruction, the patients lose their fear of childbirth and approach labor in a far more healthy and satisfactory way. It has been rare that any patient who has been managed by this group method has required more than 75 mg. meperidine (Demerol) as total sedation for labor. I think, however, the method of instruction is an individual consideration. The important thing remains that the patient asks for, and wishes to be, instructed. She wants to know what you expect of her and what she can expect of you, and of labor—and if this is done, I believe that the entire process of labor and delivery can be made more pleasant for her and for ourselves. In addition, I believe we may well tend to avoid some of the complications of labor by improving the attitude of the patient. I mean specifically the inertia problems which Reynolds believes are related to the tense and apprehensive patient.[2]

In summary, therefore, the new obstetric patient usually comes to us because she has heard about us. She meets us more than halfway, and pays high tribute in selecting us as individuals to handle the birth of her child. She is a human being and an individual. She wishes to be individualized, and treated accordingly. She wishes to establish friendship with us, and to assure her the best possible management during pregnancy it is quite necessary that good rapport, or a good patient-doctor relationship be established. This must be established in terms of the personality of the patient, and in terms of the personality of the physician. There is no constant since the two variables must integrate. Once the rapport is established, and the precepts of good obstetric care are followed, and if the patient is given adequate instruction regarding her pregnancy, labor and childbirth, the outcome stands the greatest chance of being a happy and pleasant one.

References

1. Allen, G. S.: Prenatal Care: A Classroom Approach, GP 18:109, 1958.
2. Reynolds, S. R. M.: Physiological Bases of Gynecology and Obstetrics. Springfield, Ill.: Charles C. Thomas, Publisher, 1952.

Discussion (Abstract)

Dr. Glenn W. Bryant, Louisville, Ky. Dr. Allen has presented "The New Obstetric Patient" well and I feel that we can find very little with which to disagree. Most of my discussion then will be re-emphasizing points he made in his paper.

The establishment of rapport is certainly all important. Without it the patient usually seeks another physician. Many times we are seeing a young woman who is making her first visit to a physician. We have a wonderful opportunity to establish in her mind a feeling of confidence not only for ourselves but for the medical profession as a whole. Be thorough and don't rush the patient through. Be sympathetic and a good listener. One thing Dr. Allen did not mention, be definite with the patient. When we are not, a great amount of fear is usually created for the patient.

For the family physician, class instruction of prenatal patients may be good, but as an obstetrician I feel most of our patients like individual instructions.

I have enjoyed hearing and discussing Dr. Allen's paper.

The Elderly Patient: A Challenge in Surgical Management*

WILLIAM RILEY BOSIEN, M.D., and
MARIAN KREIDER BOSIEN, M.D., *Tryon, N. C.*

The reduction of postoperative complications and in the mortality rate in elderly surgical patients is one of the satisfying developments of recent years. Not only do the authors' results amazingly illustrate these advances, but they also point to rehabilitation of the patients to a happy and useful life. The latter will need be the ultimate criterior for successful surgery.

THE GRADUALLY INCREASING LIFE EXPECTANCY in this country demands a re-evaluation of the age at which a patient becomes *old*. We see not only longevity but better health generally, in the older patient, and in many instances the physiologic age is considerably younger than the chronologic age would indicate.

We have arbitrarily chosen 70 as the youngest age in this study. This report covers 102 consecutive surgical procedures in 96 patients over the age of 70. These patients were treated at St. Luke's Hospital, a 55 bed general hospital, in the four year interval between 1954 and 1958. This study has been limited to patients undergoing major surgical procedures involving major anesthesia.

The 96 patients comprising this group were evenly divided in sex, 48 in each group.

The age distribution, as one would expect, shows the majority of patients to be in the younger age groups (Fig. 1). In this series there were no operative deaths; there were 3 postoperative deaths. It will be noted that these 3 deaths occurred in the 70 to 74 year group, and actually all were 72 years of age.

Operative Procedures

Sixty of the operations were nonelective procedures in which the indication for surgery was compelling because of danger to the patient's life. In most of these cases the optimal preoperative study and preparation could not be carried out. Forty-two of the operations were of an elective nature. In a study of this type the number of patients in whom operation was indicated but not offered because of the increased risk is significant. This was true of one patient in this series. During this time there was one patient who refused our recommendation of operation. In this series gastrointestinal surgery was the most frequent performed, and gastric procedures the most frequent of these. (The 3 deaths occurred in this group of patients.) (Tables 1 and 2.)

There were 22 hernia repairs (Table 1). It is our experience that the hernias encountered in this group were frequently large, often recurrent or of long duration, and seemed to have an increased frequency of strangulation or incarceration. A number were of the sliding variety. All of these factors make them a most difficult problem.

Operative procedures for trauma, especially those relating to hip fractures, were next most frequent (Table 3). In the patients suffering from hip fractures, we do not believe that in-

TABLE 1

TYPE OF SURGERY

Gastrointestinal	29
Trauma	24
Hernia	22
Peripheral vascular	10
Rectal	5
Pelvic	4

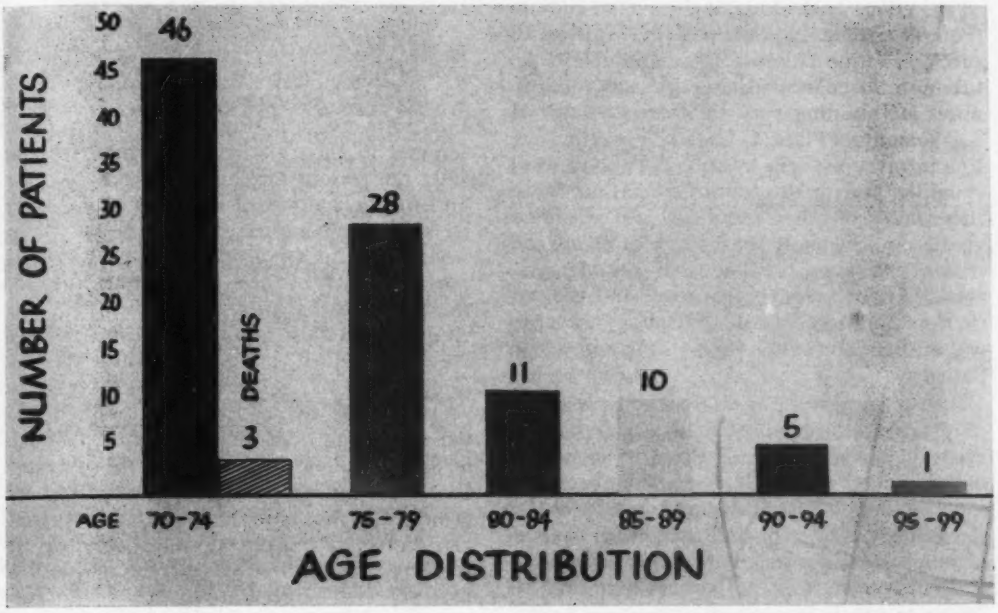
TABLE 2

TYPES OF GASTROINTESTINAL SURGERY (28 CASES)

Gastrectomy	5
P. G. E. and vagotomy	4
Cholecystectomy	5
Small bowel	6
Large bowel	4
Esophagectomy	1
Duodenal	1
Deaths	3

*Read before the Section on Surgery, Southern Medical Association, Fifty-Third Annual Meeting, Atlanta, Ga., November 16-19, 1959.

FIG. 1



serting a prosthesis is any more taxing or hazardous to the patient than fixation by a simple nail or screw. Our indications for using a prosthesis depended entirely upon the type of fracture and the possibilities for more rapid rehabilitation.

Of the 10 patients undergoing operations for peripheral vascular disease, sympathectomy was carried out on 4, amputations on 3, and a graft was used on one. It has been our hope that with increased use of arterial prostheses we would be able to reduce the number of amputations. (Since the preparation of this paper, we have added 4 patients, between the ages of 70 and 80, in whom we have used arterial by-pass grafts. There have been no deaths or serious complications. Three of the grafts seem to have been successful in preserving ambulation and the viability of an endangered foot.)

Only 8 of the 102 operations were for malignancy, a surprisingly low incidence, for which we have no explanation. In these 8 patients, efforts at curative surgery were possible in only a half, and in only 2 were these efforts successful.

TABLE 3

TYPES OF TRAUMATIC SURGERY (24 CASES)

Hip nailing	17
Hip prosthesis	4
Other	3

Anesthesia

The choice and management of anesthesia was aimed at preserving physiologic and biochemical homeostasis. The wide variations in physiologic age among geriatric patients demand that anesthesia be managed accordingly. All patients were given light premedication, with the exception that they received greater amounts of atropine, usually 0.6 mg. (gr. 1/100). The physiologically younger geriatric patient does well with a wide variety of types of anesthesia. The precautions used in this group were those used in the management of any good anesthesia with emphasis on minimal dosages of drugs.

In table 4 the group of cases labeled "ether"

TABLE 4

TYPE OF ANESTHESIA

Pento-N_2O suc.	62
Spinal	28
Ether	10
Field block	2

for the sake of simplicity, received in addition to the ether, small doses of thiopental sodium (Pentothal) for induction, then intravenous succinylcholine chloride for endotracheal intubation. After intubation, ether was administered maintaining very light levels, Stage II and sometimes Plane 1. Usually a succinylcholine intravenous drip was necessary to prevent coughing and/or to produce relaxation. With these levels of ether anesthesia and adequate ventilation, hypotension is not a problem, the patient remains physiologically stable, untoward reflexes are seldom seen, and the patient awakens quickly. This type of anesthesia was reserved for some of the younger geriatric patients.

The older geriatric patient has a markedly diminished ability to adjust to change and is easily depressed by small doses of narcotics, sedatives, and anesthetic drugs. For these reasons the most commonly used anesthesia in this group has been nitrous oxide with the use of a muscle relaxant when necessary. Adequate oxygenation must be maintained by means of adequate ventilation, usually assisted or controlled, as well as a proper concentration of oxygen. Therefore, in most instances these patients have been intubated after a small dose of Pentothal and the necessary amount of succinylcholine. Following intubation anesthesia can frequently be maintained with nitrous oxide and, as necessary, succinylcholine. At times, further small increments of thiopental or possibly meperidine HCl are used as required.

Spinal anesthesia is well tolerated in the aged only if the anesthetic level is kept quite low. With sympathetic blockade comes the danger of serious hypotension which is not only difficult to control, but also very poorly tolerated by the older geriatric patient.

Local and regional anesthesias are very satisfactory in certain instances, but it must be remembered that the old patient has a diminished ability to detoxify the drugs used.

The great danger during the recovery period is that of severely depressing the patient with narcotics. Many times the very old patient will not complain of pain unless specifically questioned and he will respond to very small doses of narcotic or analgesic drugs. Therefore these drugs are not given unless they are definitely needed and then are used sparingly.

Discussion

When we first began caring for this group of elderly patients, we had fears and forebodings of poor results. As some time passed and we began to be impressed with the good results we were obtaining, we became more interested in these patients and began to consider the reasons for these results. Since then, and in our analysis of the cases at this time, we have been impressed with certain factors which we think are quite important. Certainly one of the first of these, and perhaps the most important, is that these patients must be relatively free of disease to have attained this age. As we mentioned before, our 3 deaths occurred in the 70 to 74 age group. We have been impressed with the considerably greater incidence of complications and higher incidence of deaths among the patients in the age range from 62 to 68. It is particularly in this younger group that we have encountered disastrous cardiovascular complications, at times involving renal failure. We suspect the majority of patients with severe cardiovascular problems have fatal complications before reaching the age of 70.

Other factors which are considered most important in successfully carrying out surgical procedures are correction of any pre-existing diseases as completely as possible, and meticulous attention during the operative and postoperative period to the most minute details.

The most common pre-existing disease has been arteriosclerotic heart disease (Table 5). Electrocardiograms and roentgenograms of the chest should be obtained in all of these patients. These and other studies, as well as the consultation of an internist, can be very helpful in evaluating the cardiovascular status, but in our experience the most informative has been a careful history of the patient's exercise tolerance. Where the tolerance has been good and the patient has been active, little diffi-

TABLE 5

PRE-EXISTING DISEASES

Arteriosclerotic heart disease	24
Pulmonary diseases	8
Electrolyte imbalance	7
Obesity	8
Diabetes mellitus	2
Recent cerebrovascular accident	2
Recent myocardial infarct	2
Combination	15

culty has been encountered despite some rather alarming levels of blood pressure, electrocardiographic tracings and cardiac silhouettes on x-ray. A varying policy on digitalization of these patients has been followed. At the present moment it is thought that all patients who are in obvious cardiac failure, those with significant conduction defects on the electrocardiogram, and those with cardiac enlargement by x-ray should be digitalized. Patients with an increased blood or plasma volume have recently been added to these.

In the treatment of pre-existing pulmonary diseases, mechanical measures, such as postural drainage, good oral hygiene, and the use of effective expectorants have been most helpful. Steroids and antibiotics would seem to be of little value except where specifically indicated.

Electrolyte imbalance is one of the most easily corrected pre-existing problems and is one of the most disastrous if unrecognized. In any case where there has been vomiting or other unusual loss of body fluid, the sodium, potassium, chloride, and carbon dioxide values should be checked prior to operation. These can be very rapidly corrected using concentrated solutions of the appropriate electrolytes. No difficulty has been encountered in giving as much as 800 mEq./L. of sodium, potassium, or chloride in as little as 500 cc. fluid. The improvement of the patient's general condition following such therapy has often been dramatic. In many situations in which steroids and various vasopressors are used empirically, further investigation would reveal various electrolyte imbalances, the correction of which would make unnecessary the use of other measures.

The problem of obesity, while not very common, perhaps because obese people do not live this long, is one about which little can be done. In the elective cases attempts to induce these patients to lose weight have been unsuccessful.

It is much easier to prevent complications from developing than to treat them after they occur. The incidence of pneumonia and phlebothrombosis with embolism has been quite low in this series (Table 6). In the prevention of pneumonia, one of the most important factors is a thorough endotracheal toilet as secretions collect throughout the operative procedure. At the conclusion of the anesthesia, this should be repeated taking care not to produce atelectasis by over-vigorous suctioning. At times it may be necessary to pass a sterile catheter through the larynx and aspirate the trachea postoperatively. While bronchoscopy can be helpful, it has been found to be of temporary benefit. Usually the simple procedure of encouraging the patient to cough vigorously will be far more effective. This cannot be entrusted to the nurses. Preoperative reassurance that wounds will not disrupt frequently make patients much more cooperative in this effort. Using these methods, tracheotomy has not been necessary in any of these cases.

TABLE 6

COMPLICATIONS

Electrolyte imbalance	10
Pneumonia	6
Phlebothrombosis and embolism	0
Coronary occlusion	4
Cerebrovascular accident	1
Urinary retention	14
Hernia of wound	0
Dehiscence	0

In the prevention of both pneumonia and phlebothrombosis, early and vigorous ambulation is necessary. As soon as the patient awakens from the general anesthesia or recovers from the spinal anesthesia, vigorous action of the legs and ankles in bed is encouraged. The following day a program of ambulation is initiated. Dangling is forbidden and is considered to be predisposing to thrombus formation. As an initiation at ambulation the patient is "walked" on a stool at the bedside in the company of the nurse and attending physician. At least fifteen steps in place are encouraged. The patient is much more willing to cooperate in this if his physician is with him the first time. After it has once been demonstrated, he is willing to "walk" with the nurses, and this should be done at least four times a day. This regimen has definite advantages. (The patient need not put on a bathrobe, since the extra exertion involved can be quite fatiguing.) This procedure reassures the patient that if he should become weak or faint he is close to the bed and can get back without any difficulty. Patients wear their regular street shoes for this ambulation, because walking in bedroom slippers or bare feet will frequently result in an arch or muscular strain which is difficult to differentiate from a phlebitis. In the prevention of phlebothrombosis

it is also important that the bedcover not be drawn too tightly over the patient's feet (again causing muscle strain) and that the bed not be flexed at the knee level, thereby cutting off venous circulation at both the level of the knee and the thigh. In our group of patients none have had a presumptive diagnosis of phlebothrombosis and consequently none have had anticoagulant therapy. Prophylactic anticoagulants were not used. Prophylactic superficial femoral vein ligations were carried out in all amputations and in 2 other patients in whom it was thought postoperative ambulation would be inadequate.

Electrolyte imbalance can be easily prevented, if one carefully follows the losses incurred by the patient. At times the electrolytes must be checked as frequently as every 4 to 8 hours, since they can change quite rapidly and should be compensated for promptly. When indicated, spot checks are made on the electrolyte content of the urine, nasogastric drainage, and other fluid losses of the patient in an effort to determine how much potassium, sodium, and chloride are being lost. Once these are ascertained for a patient, they remain relatively stable over a period of several days.

The prevention of dehiscence and infections of the wound is important and it is believed that meticulous attention to fundamental surgical principles is most important. The blood supply of the tissues is frequently diminished in these patients. Small bits of necrotic tissue which remain in the wound, or rough handling of tissues will not be tolerated as it will in a younger patient.

One procedure that is being used more extensively is the determination of blood volume by radioactive serum albumin and chromium tagged red cells. This, as a preoperative base line, permits adequate correction of blood volume preoperatively and is used in conjunction with weighing all blood loss both in sponges and in the suction battle. This permits immediate replacement during and following operation.

One of the secrets of successful prevention of many complications is acceptance of the responsibility for these things by the surgeon. Certainly no one enjoys many of these tasks, but all too often if they are entrusted to nurses or nurses' aides they are not done correctly, or done at all.

The 3 deaths occurred in the patients who had operations for gastrointestinal disease.

The first case was that of a patient who had extensive carcinoma of the prostate with invasion of the bladder and rectum causing very severe pain. The patient was desperate for relief of pain and so much wanted to live without the unpleasant effects of large doses of narcotics that, under the persuasion of the family physician and the patient himself, a pelvic exenteration was undertaken. The patient developed severe electrolyte disturbances which he did not survive.

The second case was that of a man with a pyloric stenosis. He was in extremely poor condition but the obstruction could not be relieved by conservative methods. The Levine tube was removed on the third postoperative day and, after initially taking foods and fluid well, he apparently developed either gastritis or edema of the stoma, resulting in some regurgitant vomiting with aspiration. This aspiration produced a fulminating pneumonia from which the patient expired.

The third patient had mesenteric thrombosis with inadequate resection of the bowel, further gangrenous change in the bowel, and disruption of the suture line resulted in fatal peritonitis.

In all 3 cases the terminal event actually was uremia due to renal failure. While this was not mentioned as one of the complications it is a frequently encountered problem. Usually it was thought to be secondary either to cardiovascular disease or to electrolyte imbalance. The circulation to the kidneys and renal function are often quite marginal in older patients and minor disturbances of these factors may precipitate complete renal failure.

Finally, someone may ask us, as we have frequently asked ourselves, "What is the point of surgical attempts to salvage these people?"

TABLE 7

SURVIVAL FOLLOWING SURGERY

	Follow-up	*Dead*	
2 months	7	1	
6 months	20	10	
1 year	23	5	
2 years	27	1	
3 years	15	2	
4 years	11	0	
Still living		68	71%
Dead		28	29%

TABLE 8

REHABILITATION FOLLOWING SURGERY

Useful life	59	61%
Questionable	20	21%
Invalid	14	15%
Dead	3	3%

Occasionally, it has been our experience to carry out an operation successfully on such a patient, only to find that everyone in the family was hoping for an early death so they might be relieved of the burden of this aged person. Our follow-up study is illustrated in table 7, and it will be seen that in this short time we have had at least 26 patients who have survived for a period of three or four years and an equal number who have now survived two years beyond their surgical procedures.

An evaluation of what they did with their lives after the surgical procedure is difficult. However, we have tried to analyze this problem objectively (Table 8). It is believed that approximately 60% of these patients had useful and enjoyable lives; 20 apparently did not or were difficult to evaluate, and 14 were permanent invalids following operation. Several of these 14 were invalids prior to our operative procedures.

Summary

In summary, we have presented 102 cases of major surgical procedures in 96 patients, 70 years of age or over, with a mortality of 3 per cent. In our opinion the most important factors in this study have been the inherent good health of the patient, the correction of preexisting disease, the prevention of complications, and the personal attention on the part of the surgeon to the details of the patient's care.

Addendum

Since the preparation of this manuscript 38 additional patients over the age of 70 have had major surgical procedures with one death.

Discussion (Abstract)

Dr. Willard H. Parsons, Vicksburg, Miss. To my knowledge, Dr. Bosien has just reported the lowest mortality for major surgical procedures on elderly patients that has appeared in the American literature. One must congratulate him, at the beginning of any discussion, upon his superb results.

This is a subject in which I have been interested for many years. On several previous occasions my associates and I have reported our experiences with major surgical procedures in elderly patients. Up to this time we have put on record 1,049 consecutive major operations on patients in this age group, with a gradual reduction in our case fatality rate from 14.7 to 8.2 per cent. The reduction, while gratifying, still leaves much to be desired and is far short of the results Dr. Bosien has just presented.

In reporting any type of surgical results, certain categories should be considered. Our mortality for elective procedures has varied from 8 to 5 per cent. Our mortality for procedures done as a matter of immediate necessity has gradually fallen from 18.1 to 9.0 per cent. The case fatality rate for operations done for malignant disease has fallen from 33.3 to 14.8 per cent. It is rather surprising that Dr. Bosien encountered only 8 instances of malignant disease in his 102 cases. We encountered 322 major malignant processes in our 1,049 patients, more than 30 per cent.

As for anesthesia, while we use spinal less and less frequently, it is our opinion that it is not the agent used but the skill of the anesthetist which decides the patient's fate. The elderly patient, of course, should not be oversedated, and barbiturates should be avoided. Hypoxia is an invitation to disaster.

Elderly patients do not tolerate Levin tubes well, and I have often wondered whether it might not be better to resort to temporary gastrostomy than to leave an indwelling tube *in situ* for a matter of days.

One of Dr. Bosien's more important observations was that it is far easier to prevent complications than to care for them once they have developed. They must be avoided both before and after operation. Staged procedures also should be avoided.

Dr. Bosien had no deaths from embolism. He is fortunate. We insist upon early ambulation and use all the other measures known to us to prevent this highly lethal complication, but we still encounter it.

I am sure that Dr. Bosien will agree with me that elderly patients do not submit well to any changes in their regular habits. Their psychologic care is therefore of paramount importance. Without such care they may become truculent, which is bad, or lose their will to live, which can easily be fatal.

Dr. Bosien's outstanding results must be attributed to very careful preoperative studies, to dexterous surgery and to a humane, as well as a scientific, understanding of his patients' problems. Again I congratulate him.

The Staphylococcus Problem on a Single Dermatologic Ward: Charity Hospital—January-June 1959*

C. BARRETT KENNEDY, M.D., A. E. CAROE, M.D., and V. MEDD HENINGTON, M.D.,† *New Orleans, La.*

Because the staphylococcus has been so much in the eyes of the medical profession as related to hospital infections especially, the authors made a survey of its presence in skin lesions on the dermatology ward of Charity Hospital. Extensive studies showed that many staphylococci were isolated, but strains varied greatly and made virulence unpredictable.

DESPITE MUCH INTENSIVE WORK in the past few years, the basic aspects of staphylococcal infections are still poorly understood. The wide yet continuous spectra of both host resistance and characteristics of bacterial strains are the prime obstacles to this study. Investigation of staphylococcal participation in diseases of the skin is especially difficult. The entire problem has been adequately summarized by Blair,[1] and Pillsbury and Kligman.[2]

Our interest in the problem was stimulated by the occurrence of a mild outbreak of folliculitis and furunculosis on the colored male ward at Charity Hospital in late January 1959. At first the problem seemed to be simply one of tracing the infection and its mode of spread from patient to patient. As we reviewed our observations, many interesting facets of the staphylococcus problem began to present themselves. Some of these we attempted to study on a small scale over a four month period. In short, we have made a limited study of a single dermatology ward, attempting to correlate the clinical and bacteriologic state of patients.

Methods and Materials

A comprehensive chart was maintained on the bed assignment, clinical condition and therapy of every patient on the colored male dermatology ward at Charity Hospital. The study extended over a four month period. Specimens for bacteriologic study were periodically obtained from patients who were thought likely to require hospitalization for at least one week. Furuncles and unruptured abscesses selected for study were lightly cleansed and sponged with 70% alcohol. The skin was allowed to dry. Tuberculin syringes with small bore needles were used to obtain purulent material for smear and culture. In eczematous or openly purulent process, the skin was not cleansed prior to obtaining smears and cultures of the area. Sterile cotton tipped applicators were used for this purpose. Materials for smear and culture studies of vectors were obtained by direct application of moist sterile swabs to the object being studied. Direct smears of specimens were examined in most cases. Specimens were either inoculated primarily into brain-heart infusion broth, or plated immediately on rabbit blood agar. Aerobic cultures were done exclusively. Plates were examined at 24 and 48 hours. Staphylococcal colonies were identified tentatively and subcultured. Culture plates from which identifiable staphylococci could not be isolated were discarded. Streptococci at times were mistaken for staplylococci on primary isolation. Morphologic characteristics after incubation in broth culture for 24 hours were always sufficient to resolve identification of these microorganisms, however.

Coagulase testing was done by the method of Cadness-Graves and associates,[3] and the tube method, the latter being accepted in case of discrepancy. Sensitivity studies were done with the following antibiotics: penicillin,

*Read before the Section on Dermatology and Syphilology, Southern Medical Association, Fifty-Third Annual Meeting, Atlanta, Ga., November 16-19, 1959.

†From the Department of Dermatology, Louisiana State University School of Medicine, New Orleans, La.

TABLE 1

ARBITRARY GROUPING OF STAPHYLOCOCCAL CULTURES

Group I	Staphylococci which were believed from clinical observation to be contributing definitely to disease process of the skin.
Group II	Staphylococci isolated from skin. These were definitely not causing immediate pathologic effects.
Group III	Staphylococci isolated from lesions of skin in which the pathogenic effects of the bacteria were questionable.
Group IV	Staphylococci from a common environment to patients: bathtub, air plate, etc.

streptomycin, chloramphenicol, tetracycline, novobiocin, erythromycin, ristocetin, neomycin, kanamycin, and bacitracin, using a modified agar diffusion method. A dilution of 10,000 gamma per cc. of ristocetin was used; a dilution of 1,000 gamma per cc. of all other antibiotics was used. The disk method was not employed. Effects on a control staphylococcus were studied on every plate tested. If effects on this control organism were dissimilar, the sensitivity study was repeated. Phage testing was performed by the Louisiana Department of Health in accordance with standard methods. The following staphylococcal phages were used in this series: 29, 52, 52A, 79, 80, 3A, 3B, 3C, 55, 71, 6, 7, 42E, 47, 53, 54, 73, 75, 42D, 87, 83(VA4), 44A, and 81.

Results and Analysis

Summaries of findings are presented in accompanying tables. Specific instances illustrating general findings are incorporated in the paper.

One hundred and forty-seven separate isolations of staphylococci were made. Identification was made according to the criteria described by Topley and Wilson.[4] Cultures were arbitrarily grouped into four categories in the manner indicated in Table 1.

Selection for the groups was made on clinical grounds, with aid of results of microscopic examination of direct smears in doubtful cases.

Group I consists of 57 cultures taken from 6 patients who were judged clinically to have bacteria actually playing a role in the disease process. Identifying data and clinical diagnoses of these patients are listed on table 2.

Group II comprises 17 cultures of staphylococci from 3 patients in whom it was almost certain that bacteria were not playing a pathogenic role in the skin. These patients are listed in table 3, with other accompanying information.

Group III consists of 30 cultures from 9 patients in whom the participation of bacteria in the disease process of the skin was questionable. Individual patient data are presented in table 4. Smears and cultures were taken from the area of dermatitis in these patients.

Group IV consists of 36 cultures taken from the "background" or environment common to all those on the ward. Exposure of all patients to these staphylococci (isolated from air and toilet facilities) could be expected. Cultures taken from the area of the "ring" of the tub could usually be expected to show staphylococci on culture, and usually scattered cocci on smear. After use by a patient, the tub is washed out by an attendant with Phenolor compound, but several hours afterward a flourishing growth of staphylococci in the "ring" is noted. Table 5 gives a resumé of these cultures and source.

TABLE 2

PATIENTS' CULTURES PLACED IN GROUP I

Patient	*Initials*	*Age*	*Dates of Admission—Discharge*	*Diagnosis*	*Number of Cultures*
1	W.A.	72	1/16-1/31	Contact dermatitis; later multiple furunculosis	2
2	S.S.	63	1/7-1/26	Stasis eczema; overtreatment dermatitis; furunculosis	1
3	O.StC.	68	1/9-2/5	Planing; furunculosis	4
4	W.M.	51	1/10-3/7	Xanthoma tuberosum; furunculosis	5
5	N.S.	56	2/19-date	Exfoliative dermatitis, furunculosis Staphylococcus bacteremia	27
6	W.B.	59	4/6-4/20	Contact dermatitis with definite superimposed infection	18
				TOTAL	57

phages have been found. Eight coagulase negative organisms whose morphologic characteristics and antibiotic patterns seemed identical to other isolated coagulase positive organisms were phage-tested by the Louisiana Department of Health by special request. All of these were "untypeable" as expected. The reason for the predilection of the thus-far discovered phages for coagulase positive organisms is not apparent at present.

In agreement with other authors,[13] we found a preponderance of alpha-hemolysin producing organisms in the group in which we believed that bacteria were playing a pathogenic role (Group I). We believe, however, that at least occasionally, nonhemolytic staphylococci can produce pathogenic effects in skin.

Miscellaneous Observations

In a large series Livingood and collaborators[14] failed to find a single instance of bacitracin-resistant staphylococci following topical use of bacitracin. We were able to isolate from the leg of a patient, D. G., a coagulase negative nonhemolytic staphylococcus. This organism was completely resistant (in the dilutions tested) to penicillin, streptomycin, chloramphenicol and tetracycline. It was sensitive to novobiocin, ristocetin, neomycin, and kanamycin, and partially resistant to erythromycin. In the tube dilution test, this organism showed growth at 24 and 48 hours at 100μ./cc. but no growth at level 200μ./cc. of bacitracin. Although it seems doubtful that this organism was actually contributing to the disease process, it seems likely that development of resistance to bacitracin may actually have occurred in this case. In a second case a staphylococcus of golden color but coagulase negative was isolated from an opened jar of bacitracin ointment. This staphylococcus was resistant to penicillin, streptomycin, chloramphenicol, tetracycline, novobiocin and erythromycin. In the tube dilution test it was resistant to 25μ./cc. but not to 50μ./cc. of bacitracin.

The skin of patient No. 9, C. H., suffering from the edematous phase of generalized scleroderma, was cultured repeatedly (left forearm) over a two week period. Although the patient seemed to maintain good hygiene, *Proteus sp.* organisms consistently overgrew coccal organisms. In no other instance did this occur.

Passage of infection by means of the bed clothing was not noted in our series. Not one patient who moved into a bed that had contained an infected patient later showed evidence of infection with similar organisms. This was due perhaps to the rather stringent prophylactic system in force by the nursing service. Following discharge of any patient, beds, mattress, and mattress covers are scrubbed thoroughly with strong phenolic solutions.

Patient No. 18, J. M., was a tragic example of one of the dangers of steroid therapy. This patient, admitted for an acute generalized bullous eruption, probably bullous pemphigoid, was on high doses of steroids for over one week. On April 23, 1959, he expired quietly with few premonitory symptoms. At autopsy he was found to have beta streptococcal septicemia with widespread visceral involvement. Staphylococcal bacteremia was found in only one patient in our series, No. 6, N. S. Bacteremia in this patient has generally appeared at times when considerable weeping of seropurulent material occurs from flexures. At these times effective antibiotics have alleviated the drainage and greatly benefited the patient. This man has had a steadily worsening idiopathic generalized exfoliative dermatitis for over a year. No lymphoma has been found, although we suspect that this may be the final outcome.

Four repeated failures of staphylococcal isolation from the skin lesions of a patient were noted. The patient, a young colored man with evidence of early dissemination of long-standing discoid lupus erythematosus, had repeated cultures made from the area of the well-marked facial lesions. No bacterial growth occurred on four separate occasions. The patient subsequently showed positive L.E. preparations although several previous examinations had been negative for L.E. cells.

One of the mechanisms we postulated for the spread of infection from one individual to another was the spread through ointments. It is known that on this ward, on a number of occasions, patients receiving benefit from a particular ointment would offer to share their remedy with another patient whose progress was not as swift. A number of "hand-me-down" near-empty jars of ointments, none of which seemed to have a single owner, were

TABLE 9

STAPHYLOCOCCI ISOLATED FROM OWNERLESS OPENED OINTMENT JARS
(Measured in Mm. of Inhibition)

Culture Number	Date	Vector	Color	Coag.	Hemolytic	P*	S	C	T	No.	E	R	Ne	K	B	Phage
11	1-30	Bacitracin ungt	Ivory	Neg.	Sl.	4	0	0	0	30	3p	10	20	22	4p	"untypeable"
25	2-20	Aquaphor	Albus	Neg.	No.	7	0	0	0	16	3	8	16	18	12	not done
26	2-20	3% crude coal tar in Aquaphor	White	Neg.	No.	4p	0	3p	0	18	20	12	22	25	22	not done
28	2-24	Aquaphor	Ivory	+	Yes	0	0	18	0	25	23	5	2p	12	15	"untypeable"
40	3-11	Aquaphor	Ivory	+	Yes	0	0	ND	0	22	6	6	7	7	10	"untypeable"
42	3-14	Sulphur in Aquaphor	White	Neg.	Sl.	35	10	ND	25	25	25	12	16	10	16	not done
56	3-31	5% Hydrocortisone in Aquaphor	White	Neg.	No.	30	10	19	22	15	8p	6	12	16	13	not done
165	6-15	Calamine Lotion	White	Neg.	No.	25	20	20	20	20	31	24	28	25	28	not done
168	6-15	Crude coal tar in Lassar's paste	Golden	+	?	0	2	0	14	18	5	5	8	8	11	7, 42E,

*See footnote table 7.

cultured to ascertain whether the pattern of staphylococcal growth matched that of any particular individual (Table 9). These cultures were not placed into any of the four groups mentioned above. In only one instance could this correlation be done (Table 10).

Most of these organisms were coagulase negative and could not be seen on direct smear. Several unopened jars of ointments received from the Charity Hospital Pharmacy failed to grow out staphylococci.

Comment

The danger of error in relying on the antibiotic pattern alone in determining the identity of staphylococci is illustrated in comparing two organisms isolated from a single patient on the same day. (See Table 10,A.)

One organism was isolated from the nasopharynx, the other from a weeping oozing area in the popliteal area of a patient with exfoliative dermatitis. Smears of the latter exudate revealed many neutrophils and cocci, some of which were intracellular. Although the morphologic characteristics and "antiobiogram" were almost identical, the two organisms showed a differing phage type one to another. In a similar pattern, two Type 53, 77 organisms isolated (Table 10,B) from the same patient (with secondarily infected contact dermatitis of face) showed a markedly differing sensitivity pattern between the

TABLE 10

Culture Number	Patient or Vector	Color	Coag.	Hemolytic	(Measured in Mm. Inhibition) P*	S	C	T	No.	E	R	Ne	K	B	Phage
155	Albert Rock	Aureus	+	+	0	0	0	10	17	4	7	8	11	10	7, 42E 47, VA4
168	3% crude coal tar in Lassar's paste	Aureus	+	+	0	2	0	14	18	5	5	8	8	11	"

*See footnote table 7.

TABLE 10, A and B

NECESSITY FOR PHAGE TYPING BEFORE ASSUMING IDENTITY OF STAPHYLOCOCCI:
NECESSITY FOR OBTAINING ANTIBIOGRAM OF IDENTICAL PHAGE TYPE
STAPHYLOCOCCI BEFORE ASSUMING IDENTICAL ORIGIN

Date	Culture Number	Patient	Coag.	Hemolytic	Color	(Mm. of Inhibition) P*	S	C	T	No.	E	R	Ne	K	B	Phage
(A)																
6-1	132	(Weeping purulent dermatitis N.S.)	+	+	aureus	0	0	0	0	17	5	0	7	6	12	VA4
6-1	133	(Nasopharynx N.S.)	+	+	"	0	0	0	0	16	4p	0	7	6	13	? "untypeable"
(B)																
6-1	130	W.B. (Pt. No. 6)	+	+	aureus	20	5	8	4	15	12	3	3	8	8	53, 77
6-1	131	"	+	+	"	0	0	0	0	16	5	0	3	9	10	53, 77

*See footnote table 7.

organism isolated (1) from nasopharynx, and (2) organism isolated from the purulent area on the face.

In the opinion of many, the separation of staphylococci into pathogenic aureus types and nonpathogenic albus and citreus types is difficult. This becomes more apparent when one studies the qualities which are supposed to separate the pathogenic from the nonpathogenic staphylococci. Some recent criteria of virulence, such as survival time of staphylococci after leukocytic phagocytosis, are promising in principle but cumbersome to perform. It is apparent that no test of virulence *(in vitro)* will ever be absolute. A few individuals with poor defense mechanisms will always fall prey to the most innocuous of microorganisms.

Conclusions

1. Host factors are probably the most important in determining whether staphylococci actually invade tissue and produce signs of disease.

2. No single test of virulence yet described separates "virulent" from "nonpathogenic" staphylococci.

3. Identification of staphylococci must rest on a gamut of characteristics. Antibiograms alone are insufficient to establish identity of staphylococci in epidemiologic study.

4. Outbreaks of seemingly clinically identical hospital infections even in a single ward may not be due to a single organism.

Acknowledgment

We wish to express our thanks to the following for technical advice during the course of this study: Harry E. Dascomb, M.D., and Miss Maureen McGinn of the Department of Medicine, L.S.U. School of Medicine; Miss Lucille Godelfer, Louisiana State Department of Health and Dr. George H. Hauser, Director.

References

1. Blair, J. E.: Factors Determining the Pathogenicity of Staphylococci, Ann. Rev. Microbiol. 12:491, 1958.
2. Pillsbury, D. M., and Kligman, A.: Some Current Problems of Cutaneous Bacteriology, Modern Trends in Dermatology. New York, Paul B. Hoeber, Inc., 1954.
3. Cadness-Graves, B., Williams, R., Harper, C., and Miles, A.: Slide Test for Coagulase-positive Staphylococci, Lancet 1:736, 1943.
4. Topley, W., and Wilson, G.: Principles of Bacteriology and Immunity. London, E. Arnold, 1955, p. 621.
5. Barber, M., and Burston, J.: Antibiotic Resistant Staphylococcal Infection—A Study of Antibiotic Sensitivity in Relation to Bacteriophage Types, Lancet 2:578, 1955.
6. Spittlehouse, K. E.: Phage Types of Staphylococcus Pyogenes Isolated from Impetigo and Sycosis Barbae, Lancet 2:378, 1955.
7. Oeding, P., and Sompolinsky, D.: On Typing of Staphylococcus Aureus: Relationship Between Typing According to Phage Patterns, Serology, and Antibiograms, J. Infect. Dis. 102:23, 1958.
8. Knight, V., and White, A. C.: Drug Resistant Staphylococci: I. Their Distribution in Hospital Patients, South. M. J. 49:1175, 1956.
9. Smith, L.: Staphylococcal Infections. Chicago, Year Book Publishers, Inc., 1958, p. 38.
10. Nelson, C. T., and McCarthy, J.: Pyodermas and Their Management, M. Clin. North America 43:869, 1959.
11. Vaccaro, H., Paredes, L., and Valenzuela, E.: In Vitro Sensitivity of 500 Strains of M. Pyogenes Isolated from Carriers to Seven Antibiotics, Antibiotics Annual, New York, Medical Encyclopedia, Inc., 1955-1956, p. 623.
12. Greer, J., and Menard, R.: Neomycin Susceptibility for Differentiating Coagulase Positive from Coagulase Negative Staphylococci, Antibiotics Annual, New York, Medical Encyclopedia, Inc., 1957-1958, p. 149.
13. Lack, C.: Biological Characteristics of Staphylococci Recovered from Pathologic Materials, Ann. New York Acad. Sc. 65:103, 1956.
14. Livingood, C., Greet, J., Burns, R., and Menard, R.: Effect of Antibiotic therapy on the Emergence of Resistant Staphylococci in Cutaneous Bacterial Infection, J. Invest. Dermat. 32:485, 1959.

Discussion (Abstract)

Dr. John H. Lamb, Oklahoma City, Okla. I wish to congratulate Dr. Kennedy upon his study of the problem of staphylococcic infections as manifested to dermatologists. The *Texas State Journal of Medicine* gave over the entire May 1959 issue to a symposium on staphylococcic infections which include:

1. A report from the John Sealy Hospital, Galveston, Tex., which showed that with an admission of 1,300 to 1,500 cases a month, 10.8 to 45.1 patients had the diagnosis of *Staphylococcus aureus* phage, 80 to 81 infections per 1,000 admissions. The mortality rate was recorded as 0.7 to 5.9 per 1,000 admissions. The classification of these patients shows that the most vulnerable of the hospital population are:

A. The very old
B. The debilitated and clinically ill
C. Those with malignancies
D. Those with diabetes
E. The blood dyscrasias
F. The severely stressed patient; for example, those with severe burns or extensive surgery.

As this article was concluded there was evidence accumulating that although the problem of hospital-acquired staphylococcic disease has been fairly well controlled, patients and personnel are carriers of the disease and are coming in from the outside with the dread organism already established in their nares or other sites of their bodies. Thus, when hospital-acquired staphylococci infection appears in the community additional measures must be taken to control the problem.

1. Bacterial cultures on hospital personnel.
2. Limit the outside visitors.
3. Treat all minor burns, cuts, and impetiginous skin lesions in and out of the hospital as potential carriers of this disease.
4. Adequate sterilization of all hospital bathtubs —with frequent bacterial cultures of the same.

The second paper on the symposium is on the importance of the presence of the pyodermas and mastitis in infants and children. These manifestations may warn the doctors of a beginning staphylococcic epidemic and may be frequent precursors of danger-

ous complications in young infants and children suffering from chronic illnesses and surgical wounds. It stresses the importance in the infant that even the mildest staphylococcic infection necessitates antibiotic therapy and that any open skin lesion, even in healthy children and adults, constitutes an abundant source of organisms which are hazardous to all whom they may contact. We wish to report an interesting case of resistant staphylococci infection in our own practice:

Mr. L. D. F., age 59, had spent several weeks in Colorado early in August 1959. Upon his return to Oklahoma he stated that he did not feel up to par. Symptoms were manifested by dizziness and malaise and the patient did not return to work until the second day of September, two weeks after his return from Colorado. He gave a history that 3 days after his return to work at the grain elevator it was fumigated with methyl bromide spray. He noted that small "bumps" began to appear behind his neck and he felt feverish. Later he developed a generalized, slightly pruritic eruption. His temperature varied from 101 to 103°. He had chills but no myalgia. This condition persisted in spite of Aveeno baths, calcium gluconate I.V. and orally, Temaril and Aristocort (the latter, of course, can alter body immune reactions). He denied any injections or other previous medications.

Examination revealed a well-developed, slightly obese white man with generalized skin eruption and acutely ill but in no acute distress. He had generalized, erythematous, edematous, slightly elevated, oval, confluent lesions ranging in size from 0.5 to 2 cm.; some showing central clearing.

Our impression was erythema multiforme (but we considered Rocky Mountain spotted fever). The white count was 13,000 with a normal differential picture except for a few atypical mononuclear cells. Blood bromide determination was negative. His B.S.P. showed normal dye retention. Agglutination tests to proteus x19 were negative in all dilutions; proteus 0x2 showed a slight positive in 1:20 dilution.

He was placed on triple-sulfa compound and tetracycline HCl tablets 250 mg. 4 times a day, with Aveeno baths morning and evening. On September 21, although the patient's generalized eruption was much improved, he began to develop boils over the entire body. These pustular lesions were deeper and more abundant around the genitals, buttocks and under the arms. In our private office his organism *Staphylococcus aureus* was tested to various antibiotics. These tests showed sensitivity to ristocetin (Spontin), nitrofurantoin (Furadantin), novobiocin, neomycin, carbomycin (Magnamycin) and chloramphenicol, but were resistant to penicillin, tetracycline HCl (Achromycin) (which he was taking), erythromycin (Erythrocin), tetracycline, oleandomycin, oxytetracycline HCl (Terramycin), streptomycin, dihydrostreptomycin and all the sulfanilamide compounds (which he was also taking). Thus, all of his previous antibiotic treatment, penicillin, triple-sulfa and tetracycline HCl were of no avail. His general condition had become much worse, his color was bad, his temperature ranged from 103 to 104°. His WBC. was 19,200 with many eosinophiles in the differential count. Because our sensitivity tests showed that the organism was sensitive to ristocetin and novobiocin he was placed on ristocetin (Spontin) 1 Gm., b.i.d. intravenously, and novobiocin 250 mg. 4 times daily. In 24 hours there was a rapid drop of his temperature from 103° to normal and it remained so for his hospital stay. There was immediate clinical response to these antibiotics and some 150 boils were resolved in 3 days. He has been well now since October 1958, and has returned to his regular work. We made a diagnosis of possible erythema multiforme, etiology unknown, with multiple furunculoses to a staphylococcus of the resistant variety. We feel that his life was saved by prompt culture and tests in our private office of this resistant staphylococcal sensitivity to the various antibiotics. It is recommended to dermatologists that this can be done easily in everyday practice with the addition of a small incubator in their offices. It may be stated that the sensitivity studies in a private office are many times much more accurate than those in a large general hospital.

We are exceedingly fortunate that each month a new antibiotic comes out which seems to cover some of these old, resistant organisms; however, we cannot be too careful even with the mildest impetigos and pyodermas in children, and it is well to culture these and perform sensitivity tests. Any chronic, ulcerative lesion, even a post-radiation ulcer, should also be cultured carefully since many times these may not be due to bacteria at all but to Monilia or some other fungi for which we have Mycostatin and now Griseofulvin. Chronic radiation ulcers in the oral cavity, in our practice, have been healed in several severe cases with an antibiotic mouth wash, the formula for which is as follows:

3 tablets aureomycin (250 mg.) soluble
3 tablets Mycostatin (100,000 units) vaginal
3 tablets cortril (30 mg.) Dissolve in
Water—120 cc.

I have enjoyed this paper by Dr. Kennedy, since this problem of resistant "staph" infections is a very important subject.

1. Hansen, Arild E.: Staphylococcal Infections, Texas J. Med. 55:335, 1959.
2. Boelsche, A. N., and Davis, Helen: Staphylococcal Pyodermas and Mastitis in Infants and Children, Texas J. Med. 55:342, 1959.

CASE REPORT

Brain Tumors in the Newborn*

R. L. DeSAUSSURE, M.D., JOE H. MILLER, M.D., and
C. E. STRICKLAND, M.D.,† *Memphis, Tenn.*

RECENT MEDICAL PUBLICITY has suggested that certain tumors develop after long periods of exposure to a carcinogenic agent. It also seems that a high percentage of neoplasms occur in the older age groups. In view of this we thought it worthwhile to report the case of a brain tumor present at birth, since any theory which is advanced to explain the etiology of malignancy must include all age groups. Our case may not fulfill the criteria of Matson,[1] who stated that "to warrant publication, a single case report should record a clinical experience sufficiently unusual and provocative to become valuable in itself to others who may encounter a similar problem." However, our case was that of a twin which may justify its publication. We are limiting the neonatal period to the first 60 days of life as has been defined by Arnstein[2] in his report.

Case Report

The patient, a 3 day old white boy, was referred to the Baptist Memorial Hospital on Oct. 21, 1957, from another city because of a swelling in the right temporal area. The patient was the first born of twins. The pregnancy and delivery were normal for both infants. The patient was thought to be normal except for a mass in the right temporal region which seemed to be increasing in size.

On admission, physiologic jaundice was present. The baby was alert and seemed to cry normally. We could not detect any neurologic deficit. There was a 5 by 4.5 by 2 cm. bulge in the right temporal area, although the skin over this area appeared normal. The mass transilluminated and was fluctuant but did not pulsate. There was slight exophthalmos on the right. The anterior fontanelle was tight. Approximately 6 hours after admission the baby stopped breathing and expired.

(A letter from the patient's parents in October 1959, indicated that the surviving twin is normal and in excellent health.)

Post-mortem skull films (Fig. 1) were made and the following is the x-ray description:

"AP and lateral projections show very definite spreading of the coronal and occipitoparietal sutures. The bones in the calvarium are much thinner than is usually seen in infancy. The right temporal frontal area showed bulging with wide separation of the parietotemporal sutures on this side. In addition, there is distortion of the right orbit due to elevation of the sphenoid wing. In the temporal region there is a soft lacey indistinct type of calcification. This type of calcification is seen in brain tumors and since the calcification would have had to have been present for quite some time, it could only be a tumor of congenital origin. The calcification has the appearance of that seen in an astrocytoma."

Autopsy was granted and performed. Following is a description by Dr. C. E. Strickland:

"At autopsy, the infant weighed 2,800 Gm. and measured 45 cm. in crown to heel length. The head was asymmetrically enlarged, and there was a right exophthalmus and a 4 cm. circular failure of closure of the right frontal, temporal, and sphenoid bones, through which a portion of the tumor had herniated. When the widened cranial suture lines were opened, the brain was found to be considerably elevated by a large tumor occupying a major portion of the right middle fossa and extending into the adjacent portion of the anterior and posterior fossae. The tumor was adherent to the dura over the base of the skull, and there was slight erosion of the center and right side of the sphenoid and occipital bones. All of the cranial nerves and major branches of the circle of Willis were free of tumor, but there was diffuse tumor infiltration of the pituitary and infuntibulum (Figs. 2-4).

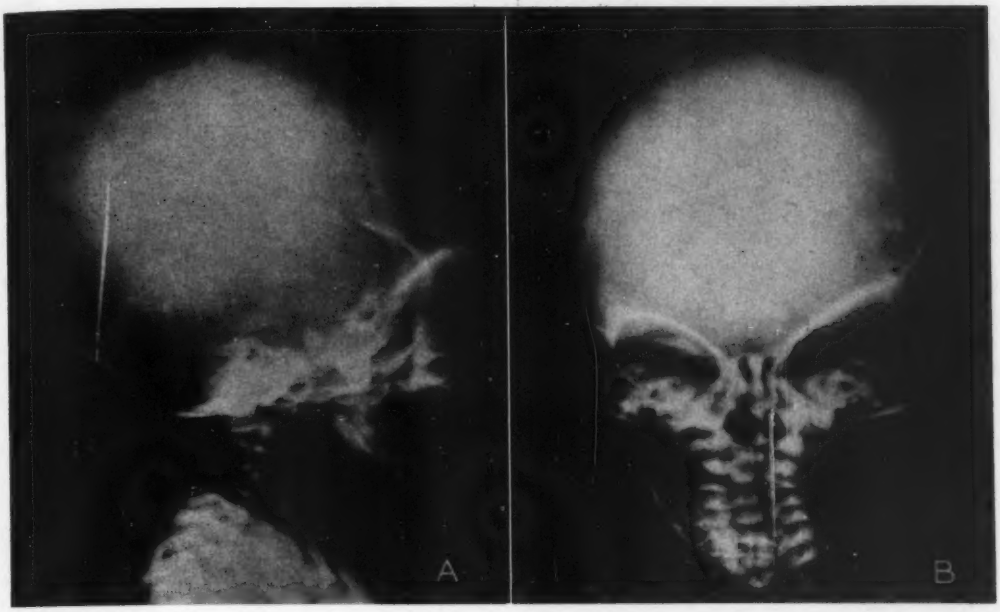
The tumor was a multilobular, spherical mass which elevated the right frontal and temporal lobes and blended into the substance of the pons and midbrain, its apparent site of origin. It measured 6 by 8.5 by 5.2 cm. and was grayish-white, glistening, and somewhat softer than the surrounding brain. Small cysts and foci of recent and remote hemorrhage were scattered at random through the tumor with the largest amount of recent hemorrhage just anterior to the pons. This tumor comprised approximately 95 Gm. of the total brain weight of 510 Gm.

Microscopically, the tumor presented a variable cellular pattern with the predominant proliferating

*Read before the Section on Neurology and Psychiatry, Southern Medical Association, Fifty-Third Annual Meeting, Atlanta, Ga., November 16-19, 1959.

†From the Department of Neurological Surgery and Department of Pathology, Baptist Memorial Hospital, Memphis, Tenn.

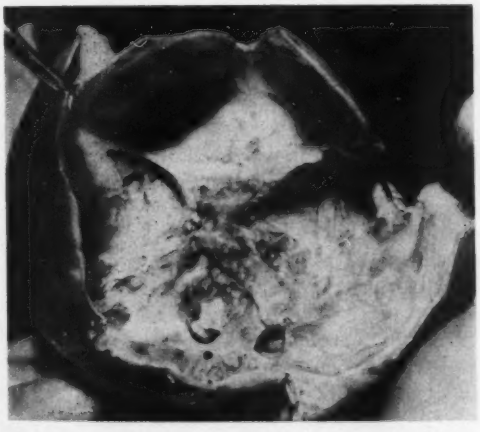
FIG. 1



cell being the mature astrocyte, which showed only slight pleomorphism. Giant cells and mitotic figures were not found, and the junction of the tumor and normal brain was indistinct. Spindle-shaped spongioblasts in streams and whorls were found in a few sections, and some of these cells had undergone mucoid degeneration giving small areas of honeycomb appearance. Microglia, small neurons, and hemosiderin-laden macrophages comprised only a small portion of the cell population. Calcification, although not recognized grossly, was an important feature of the tumor as it occurred in the media of blood vessels, as a fine granular background in areas of tumor neurosis, and as large spherioles scattered in a random fashion through the stroma.

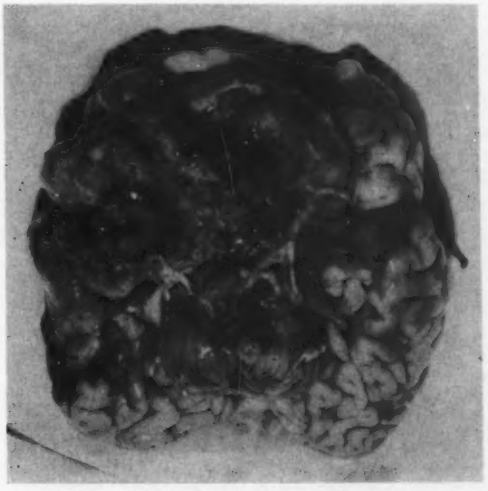
Blood vessels were prominently distributed through the tumor, and endothelial proliferation, perivascular gliosis, and perivascular hemorrhage were found in

FIG. 2



Superior view of base of skull demonstrating erosion of the sphenoid and ethmoid bones, enlargement of the right middle fossa and failure of closure of the right frontal, temporal, and sphenoid bones.

FIG. 3

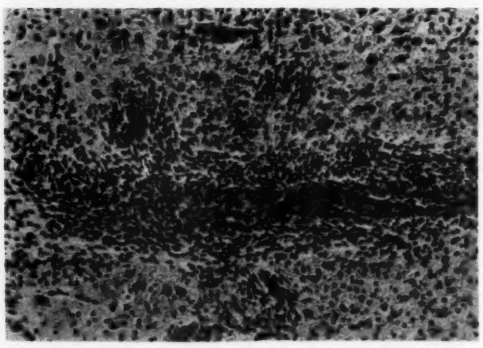


Base of brain showing the extensive tumor.

FIG. 4

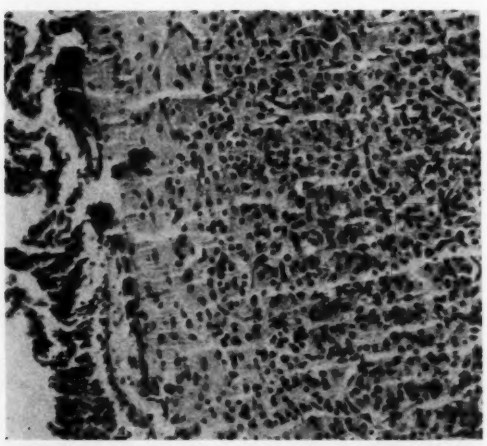
Sagittal section of brain showing origin of tumor from pons and mid-brain, cyst formation, and recent hemorrhage in the tumor anterior to the pons.

FIG. 5



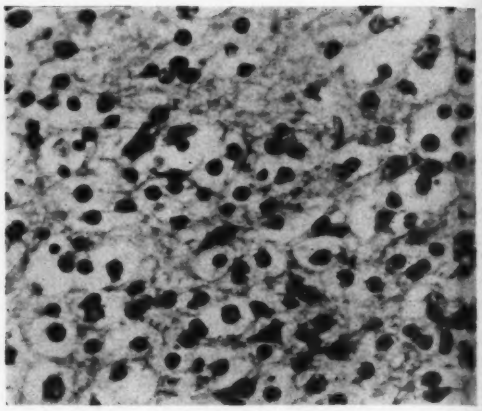
Section through the border of the tumor showing endothelial proliferation, perivascular gliosis, and increased numbers of astrocytes.

FIG. 6



Section showing increased number of well-differentiated astrocytes and focal medial calcification of intracerebral vessels.

FIG. 7



Section demonstrating honeycombing due to mucoid degeneration of spongioblastic elements.

several areas. The soft central areas of the tumor represented recent and old hemorrhages with cystic degeneration. No teratomatous or nonglial elements were found (Figs. 5-7).

Final Pathologic Diagnoses:

1. Congenital glioma, predominantly astrocytoma, Grade II.
2. Congenital macrocephaly with failure of fusion of right frontal, temporal, and sphenoid bones.
3. Exophthalmus, right, due to obstruction of right ophthalmic vein by tumor.
4. Congenital absence of left kidney and ureter.
5. Fatty degeneration of liver, mild

(Gross Specimens: Figs. 3-5.)"

Discussion

It is generally believed that brain tumors are not uncommon in children. However, the number of these reported in the neonatal period is rather limited. A review of the literature reveals 24 cases present in the newborn and an additional 13 cases in which the tumor was probably present at birth.

We do not intend to discuss the etiology of brain tumors. However, this and similar case reports tend to support the theory of embryonal rests as has been expressed by Arnstein.[2] Table 1 shows the number and type of tumors which have been found in the literature.

Although craniopharyngiomas develop from embryonal remnants it is surprising that only one craniopharyngioma in the neonatal period is reported.

Several of the case reports were found in the obstetrical literature, primarily because

TABLE 1

HISTOLOGICAL TYPES OF THE 37 BRAIN TUMORS REPORTED IN THE NEONATAL PERIOD

Type	*Number*
Teratoma	14
Papilloma choroid plexus	3
Medulloblastoma	2
Ependymoma	2
Meningioma	2
Unknown	2
Craniopharyngioma	1
Pinealoblastoma	1
Cavernous hemangioma	1
Gliosarcoma	1
Glioma	1
Polarspongioblastoma	1
Dermoid	1
Neuroepithelioma	1
Angiosarcoma	1
Cystic blastoma	1
Sarcoma	1
Undifferentiated	1
Total	37

of dystocia. Wagner[3] reported 9 cases because of difficult delivery. Seven were stillborn and one died in 30 minutes. One patient lived for 19 days. This particular brain tumor was a teratoma and inside this were 5 fetuses. The prognosis of brain tumor in this age group is rather poor, but there have been two surgical cures.[1,4] Both of these were tumors of the choroid plexus.

Summary: An astrocytoma in a 3 day old infant is reported. Thirty-seven cases are tabulated from the literature.

References

1. Matson, Donald D.: Hydrocephalus in a Premature Infant Caused by Papilloma of the Choroid Plexus with Report of Surgical Treatment, J. Neurosurg. 10:416, 1953.
2. Arnstein, L. H., Boldrey, E., and Naffziger, H. C.: A Case Report and Survey of Brain Tumors During the Neonatal Period, J. Neurosurg. 8:315, 1951.
3. Wagner, J. A., Douglass, L. H., and Slager, U. T.: Dystocia Caused by Fetal Intracranial Teratoma. Report of a Case, Obst. & Gynec. 4:647, 1954.
4. Drucker, D. A.: Papillary Tumor of the Choroid Plexus in a Newborn Infant, Arch. Path. 28:390, 1939.

PRECEPTS OF HIPPOCRATES

Sometimes give your services for nothing, calling to mind a previous benefaction or present satisfaction. And if there be an opportunity of serving one who is a stranger, in financial straits, give full assistance to all such.

For where there is love of man, there is also love of the art. For some patients, though conscious that their condition is perilous, recover their health simply through their contentment with the goodness of the physician.

And it is well to superintend the sick to make them well, to care for the healthy to keep them well, but also to care for one's own self, so as to observe what is seemly.

CASE REPORT

Staphylococcal Orbital Sepsis in Newborn Infants*

RAY HEPNER, M.D.,† *Baltimore, Md.*, and
DAVID HAGAR, M.D.,‡ *Kansas City, Kan.*

STAPHYLOCOCCAL INFECTIONS in newborn infants, and the widespread appearance of antibiotic resistant and highly pathogenic strains of this organism, have prompted increasing interest and concern.[1] In the pre-antibiotic era, staphylococcal infections of the orbit were not uncommon, and were characterized by a high mortality and morbidity.[2] With the advent of efficient antibacterial agents, and until the widespread appearance of resistant strains, the problem appeared to be solved.[3] However, case reports of staphylococcal orbital sepsis are appearing again and need for attention to the factors which lead to this serious problem exists, particularly where young infants are concerned.[4-7]

Our attention was directed to this problem by the case of C. J. R., a 17 day old infant referred to the University of Missouri Medical Center through the courtesy of Dr. John Sennott of Jefferson City, Mo.

Case Report

The patient, a white female infant, was born of an 8 months gestation with no other known complications. She weighed 5 pounds at birth, and did well while in the newborn nursery. At the time of discharge, she was noted to have a single small pustule on the thorax. Much later in the infant's course, it was discovered that the infant's hospital of birth had had a proven outbreak of staphylococcal disease due to phage-type 80/81 staphylococci. The pustule cleared spontaneously with alcohol wipes, and she continued to do well at home until the age of 12 days.

At that time the patient, the mother, father and 10 year old sibling developed a watery coryza and conjunctivitis. On the 13th day, the infant was irritable, had a purulent discharge from the left nostril, was taken to another physician, and was given an injection of penicillin. That evening, the infant had fever, was more irritable, and swelling of the left eyelids was noticed for the first time. She was admitted to her hospital of birth, and, with Panalba and streptomycin therapy, improved generally, became afebrile, and had less discharge from the left nostril. However, the left eye was worse, with more edema and erythema of the lids, and proptosis of the globe. Then she was sent by the referring physician to the University of Missouri Medical Center at the age of 17 days.

Physical examination revealed a "toxic" appearing newborn infant weighing 5½ pounds, and measuring 20¼ inches long. Her temperature was 99.8°F., pulse 136, and respirations 36. The left periorbital tissues were a deep reddish-blue color, and were markedly edematous. The lids and conjunctivae were markedly injected and edematous, with some pus in the conjunctival sac. Marked proptosis of the left globe was present, and the eye was immobile (Fig. 1). No bruit could be heard over the eye. Funduscopic examination revealed active pupils on both sides, and no papilledema, venous engorgement, hemorrhages, or cloudiness of the media. Thick mucopus was present in both nostrils, more in the left than the right. The fontanel was full but not hard, and there were no other signs of meningeal irritation. The remainder of the physical examination was within normal limits. There were no cutaneous eruptions.

Laboratory examinations revealed a Hgb. of 15.5 Gm., hematocrit of 46%, WBC. 13,950, with 55% neutrophils, 3% metamyelocytes, 36% lymphocytes, 1% monocytes, and 4% eosinophils. Repeated blood counts revealed a low of 6.4 Gm. for the Hgb. with a return to 9 Gm. before discharge. The WBC. varied from 5,000 to 9,000 during the ensuing course. Repeated urinalyses were negative for reducing substance, bile, and significant formed elements. Lumbar puncture on admission revealed 500 red cells and 2,000 white cells, 75% lymphocytes. The fluid was sterile on culture. A second lumbar puncture on the 4th hospital day revealed 5 red cells, 9 white cells (all lymphocytes), a protein of 132 mg., sugar 61 mg., and chloride 125 mg. per 100 ml., and a sterile culture.

Nose culture on admission revealed heavy growth of coagulase positive *Staphylococcus aureus*. Blood culture was sterile.

*Work done at the University of Missouri School of Medicine, Columbia, Mo.

†Now from the Department of Pediatrics, University of Maryland, Baltimore, Md.

‡Now from the Departments of Obstetrics and Gynecology and Pediatrics, University of Kansas Medical Center, Kansas City, Kan.

FIG. 1

Photographs on admission show the advanced proptosis and signs of severe inflammation.

Radiographic examination of both orbits by routine and optic foramen views on admission revealed soft tissue swelling of the left orbit and non-pneumatization of all sinuses, including the ethmoids.

The initial impression was orbital sepsis with reactive (or "neighborhood") meningitis. Treatment with chloramphenicol, 50 mg. per pound, by intramuscular injection, was instituted, along with nasal

FIG. 2

Condition at discharge more than two months later.

decongestant drops and aspiration. Three doses of superficial x-ray therapy, delivering 270 r. to the left orbit were given, and the periorbital edema seemed less by the 4th hospital day. However, on the 7th hospital day, the proptosis was not improving, and fluctuation was noted at the medial inferior aspect of the left orbit. By needle aspiration 2 to 3 ml. of thick creamy pus was obtained, and a polyethylene drain left in place. The aspirate was cultured, and proven to contain a phage-type 80/81 *Staphylococcus aureus*. By the 10th hospital day, signs of inflammation were less although still present, but little movement of the left globe could be elicited by inducing nystagmus by rotation of the patient. On the 10th day, the drain spontaneously discharged from the wound and there was no further drainage from the wound.

By the 17th hospital day, all superficial signs of inflammation of the left eye had passed, but proptosis and immobility of the globe remained. Funduscopic examination remained normal. At this time some difficulty with loose stools became evident, blue-white patches were found on the buccal mucosa of the lips and cheeks (*Monilia albicans* on smear and culture). Mycostatin therapy was begun and chloramphenicol was discontinued.

Within 4 days (on the 21st hospital day), the infant became irritable, ceased to gain in weight, and had a sudden recrudescence of edema and erythema of the left periorbital tissues. Purulent discharge again came from the left nostril. Chloramphenicol therapy was reinstituted for 8 days, with an excellent clinical response within 48 hours. Following this second course of therapy she remained asymptomatic for 6 days, and then symptoms recurred again. Radiographic examination was repeated and revealed on this, the 42nd hospital day, demineralization of the superior orbital ridge on the left, and pneumatization of the right but not of the left ethmoid sinuses. Chloramphenicol was given in the same dose per unit of weight, and a nasal shrinking agent with neomycin (Biomydrin) used intranasally. This course of therapy was continued for 22 days, and continuous improvement to full regression of edema and proptosis of the left orbital structures and purulent nasal discharge were noted. Full movement of the left eye returned without evidence of imbalance of the extraocular muscles or funduscopic abnormality (Fig. 2). She was discharged on her 68th hospital day.

She was again seen in follow-up 2 weeks later. At that time she had no evidence of ocular abnormality, by clinical or roentgen examination, and she had continued to grow and to develop normally. Meanwhile the mother had developed bilateral axillary furunculosis.

Discussion

In the preantibiotic era, the pathogenesis of orbital abscess was shown clearly to be by invasion of staphylococci from an ethmoid sinusitis.[2] Osteomyelitis of the maxilla and of the other bones of the orbit was a common complication, fistulas and sequestration with serious disfigurement were frequent. Loss of vision and even loss of the involved eye were common. Disease of tooth buds of the involved maxilla and consequent deformities of the jaw have been described. The peculiar susceptibility of infants to orbital sepsis was also emphasized before the current "staphylococcus problem" was apparent.[6] The smaller air passages, the availability and ease of infection of the ethmoids even at birth, the limited capability of the neonate to localize infections, and the natural pathway from the ethmoids to the orbit via the pterygoid veins in a plexus with sluggish flow allows easy thrombophlebitic spread.

The emergence of a highly pathogenic strain of staphylococcus which colonizes in the nose of neonates is the final stage setting for a notable return of orbital sepsis as a significant problem in young infants.[1,4]

When penicillin became available for clinical use, enthusiastic reports appeared of its efficacy in treatment of orbital infections, even with osteomyelitis.[3] Since that time, however, increasingly poor responses of staphylococcic infections to penicillin have been noted. Indeed high carrier rates for resistant staphylococci are observed in factory workers producing penicillin, as well as in hospital personnel and in patients with prolonged hospital stay. The explanation offered for these observations is that penicillin, either environmentally or therapeutically administered, destroys the normal protective microbial flora, and leaves a fertile noncompetitive ground for either the implanting or the multiplication of resistant pathogenic organisms.[1]

In 1950, a patient with a nearly identical history and course to the case reported in the present article was treated with penicillin and, just as our patient, became worse.[7] Others have reported similar experiences and have emphasized epidemiologic factors as well, particularly concurrent infections in the family—maternal breast abscess, wound infections, furuncles—and have recovered identical bacteriophage types from the infant and other members of his family.[5] In our case, adequate family studies were not made, but the infant was born in a hospital known to be having an outbreak (since controlled) of staphylococcal disease of identical phage type, she had a skin lesion at the time of discharge from that hospital, and her mother later developed furunculosis.

Summary

Staphylococcal orbital sepsis is a serious problem today, and is likely to be seen more frequently than early in the beginning of the antibiotic era.

Young infants with purulent rhinitis should be suspected of harboring a pathogenic staphylococcus.

A history of staphylococcal disease in the hospital of birth or in the family of infants with purulent rhinitis, with or without serious complications, should always be sought.

Penicillin therapy for purulent rhinitis in infancy is contraindicated, not only because it is likely to be ineffective and to delay appropriate therapy, but because it may remove the normal competitive inhibition of the pathogen involved, and allow uninhibited multiplication of pathogens.

Prolonged and vigorous therapy with antibiotics appropriate to the organisms, adequate drainage of abscesses, and especial attention to clearing the ethmoid spaces is required for successful management of orbital sepsis.

References

1. Paine, T. F., Jr.: The Genghis Kahn of the 1959 Microbial World, South. M. J. 52:1314, 1959.
2. Gamble, R. C.: Acute Inflammations of the Orbit in Children, Arch. Ophth. 10:483, 1933.
3. Jacoby, N. M., and Sagorin, L.: Osteomyelitis of Jaws in Infancy Treated With Penicillin, Arch. Dis. Childhood 20:166, 1945.
4. Lieberman, H., and Brem, J.: Acute Osteomyelitis of Superior Maxilla in Early Infancy, New England J. Med. 260:318, 1959.
5. Kerkenezov, N.: Acute Non-Specific Infection of the Orbit, With a Report of Three Cases, M. J. Australia 2:293, 1955.
6. Poncher, H. G., and Blayney, J. R.: Osteomyelitis of the Maxilla in Nurslings and in Infants, Am. J. Dis. Child. 48:730, 1934.
7. Hayden, G. D., Pastore, P. N., and Kundert, K.: Abscess of the Nasal Septum and Orbital Cellulitis in an Infant, Arch. Otolaryng. 52:773, 1950.

Meet Us in St. Louis, Mo.

Oct. 31 - Nov. 3, 1960

for

SMA's 54th Annual Meeting

Dual Bone Graft for Congenital Pseudarthrosis of the Tibia:

Variations of Technic*

GEORGE D. PURVIS, M.D., and J. E. HOLDER, M.D., *Jackson, Miss.*

Congenital pseudarthrosis is an extremely difficult lesion to correct satisfactorily. The authors emphasize the good results they have had in a small group of cases.

THE OPPORTUNITY OF TREATING 7 cases of congenital pseudarthrosis of the tibia has been a stimulating challenge. During the 9 year period over which these have been treated we have made certain observations and have evolved a variation of the technic of dual bone grafting which was developed by Boyd.[1,2] Variations such as we describe have been used by Moore[3] and other surgeons; but this procedure in two stages and in its entirety has not been reported.

The fact that the etiology of congenital pseudarthrosis is still nebulous probably contributed to the diversity of treatments and the high incidence of failures. An inter-relationship between pesudarthrosis of the tibia and neurofibromatosis is substantiated in our series by one half of the cases exhibiting either nodules of neurofibromas or café-au-lait spots. However, pathologically no such lesion was found at the pseudarthroses in this series.

The affected area was at the junction of the middle and distal one thirds of the tibia and fibula in our cases. The pseudarthrosis was present at birth or developed soon thereafter as the result of relatively minor trauma. Of the 7 patients treated, 5 were male, 2 female, 6 were colored and one was white. When first seen they ranged in age from 2 weeks to 14 years, averaging 4 years and 8 months. Three of the patients had had previous unsuccessful bone grafts.

It has been claimed that with earlier grafting less angulation, calcaneus deformity and leg shortening occur. However, it has seemed to be more difficult to obtain union in the young group. We believe that 4 to 6 years of age is the optimum age for the technic which we use. At this age the child's donor leg is large enough to supply an adequate graft without significant danger of fracture if the graft is carefully procured. At the same time, most extremities can be maintained in relatively good alignment with bracing during this age span. The average age at which surgery was performed in this series was 8 years and 8 months (Table 1).

Most of our patients were operated upon after the optimum age because they were beyond that when we first saw them.

Technic of the Operation

The first stage of the procedure is a preparatory one. The approach is by way of a curvilinear anterolateral incision giving access to the tibia and the fibula through a vascular skin flap. This prevents an adherent scar to the graft and a scar overlying the bone. The dense fibrous tissue about the ends of the tibia and the fibula are excised along with the pseudarthrosis. The sclerotic pointed bone ends are resected for a distance of 0.5 to 1 cm. and drill holes are made into the medullary canals of each fragment. If it is necessary to

TABLE 1

AGE AT TIME OF OPERATION

4 years and 4 months
7 years and 11 months
10 years and 10 months
10 years and 9 months
15 years and 6 months
5 years and 4 months
6 years

*Read before the Section on Orthopedic and Traumatic Surgery, Southern Medical Association, Fifty-Third Annual Meeting, Atlanta, Ga., November 16-19, 1959.

gain length and overcome anterior angulation, a second incision is made posteriorly along the medial aspect of the Achilles tendon. It is lengthened in the usual Z manner and a posterior capsulotomy is performed if needed. Occasionally Z lengthening of the posterior tibial and flexor hallicus longus tendons are indicated. A small Steinmann pin about 3/32 inch in diameter is then inserted in the medullary canal of the distal fragment of the fibula and drilled out the distal end through a stab wound. The fibula and tibia are aligned and the wire is drilled retrograde well into the proximal fibular medullary canal. No attempt is made to oppose the fibular ends as frequently this cannot be done because of absence of bone length. The intramedullary wire in the fibula serves as a strut to maintain general alignment between the two stages of the operation, and subsequently it helps prevent some strain on the dual graft. The distal end of the wire is bent at the distal end of the fibula and is cut off subcutaneously. The incisions are closed with skin sutures only and a long leg cast is applied. Usually in the young patients, the knee is flexed to 90 degrees and the ankle is held at 90 degrees. In two weeks the sutures are removed by way of windows in the cast. In 6 to 8 weeks the cast is bi-valved and removed twice daily for about one week for skin care.

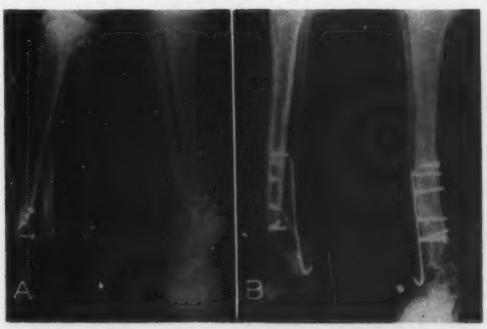
Following this the second stage procedure is performed by two surgical teams. Using a reciprocating bone saw, a full thickness cortical graft is removed subperiosteally from the child's unaffected tibia. The width of the graft is that width which can be obtained from the anteromedial aspect of the tibia without violating either pillar. The length must be sufficient to permit the graft to be cut transversely at midpoint giving grafts long enough to bridge the tibial defect and permitting insertion of two screws proximally and distally. This usually requires a graft taken from just distal to the proximal epiphysial line of the tibia to the junction of the middle and distal one thirds. Small strips of cancellous bone are taken from the donor tibia.

Simultaneously, the other team reopens the anterolateral scar, exposes the tibia and removes shavings of cortical bone from both tibial fragments to prepare flat surfaces for the application of the grafts. These are applied in the manner described by Boyd[1] as opposing struts gripping each bone end and held with a bone holding forcep. Two screws are then inserted transversely through the lateral graft, the cortices of the tibia and the medial graft both proximally and distally. The resulting trough is then filled with the cancellous strips and the skin is closed. A long leg cast is reapplied. Immobilization by cast is maintained until there is roentgenographic evidence of bone union. This period of immobilization ranged in our series from 3 months and 12 days to 7 months and 26 days, an average time of 5 months and 15 days. When the cast is discarded after there is incorporation of the graft, the leg is placed in a long leg leather lacer brace with a drop lock knee and limited motion ankle. The brace is fashioned with posterior lacing as devised and recommended by Kite[4] in 1941. The brace is worn at all times for weight bearing until at least late puberty because of the danger of fracture. Roentgenographic progress is followed at 3 to 6 month intervals. It appears desirable as recommended by several authors to reinforce with iliac grafts any areas that become thin, narrow or sclerotic.[3-5] This has been done recently in one of our older patients at the time of removal of the screws.

Results

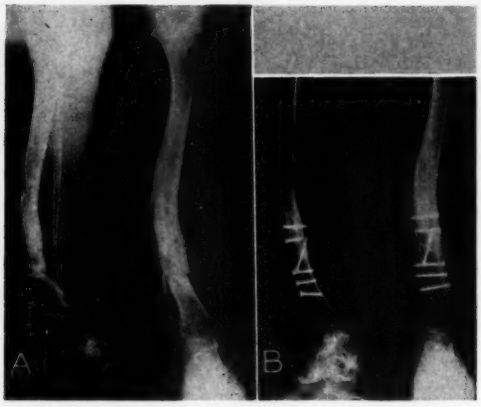
In each of the first six patients treated in this manner there has been solid union. (See figures 1-9.) The seventh has been treated within the past year and thus is too recent for evaluation, although at present it appears to have union. In two cases refracture occurred, 27 months and 5 months postoperatively. In each the bone was regrafted using donor bone from the regenerated opposite tibia. It is in-

FIG. 1



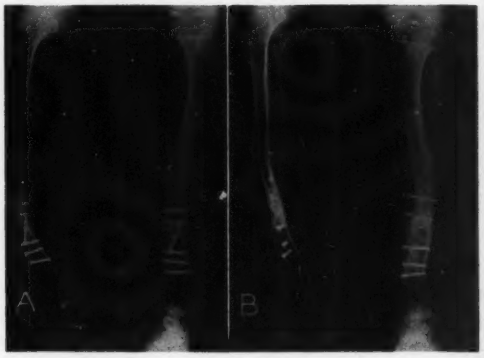
(A) Age 10 years (6 years postoperative unsuccessful single onlay bone graft). (B) Twenty-six months postoperative dual graft.

FIG. 2



(A) Age 12½ years. (B) Union 9 months postoperative grafting.

FIG. 3



(Same case as Fig. 2.) (A) Nineteen months postoperative graft showing traumatic fracture. (B) Twenty-four months postoperative second grafting.

teresting to note that intramedullary fixation of the fibula was omitted in both of these cases. In one of these, our oldest—age 14 years and 8 months when first seen by us—a skin slough occurred following the second graft. After a cross leg flap by a plastic surgeon drainage persisted. Although bone union had occurred, the patient and his family chose to have the leg amputated because of drainage, a sensitive scar and the shortened extremity. One other patient, our last, developed a superficial wound abscess which cleared with antibiotic therapy without apparent adverse effect on the grafting result. Kite[4] reported better incidence of union in that part of his series which had some infection.

One of our patients has discarded her brace at age 16 years, 8 months. This was 5 years after operation. At an unsuccessful operation

FIG. 4

(A) Age 6 years. (B) Four years and 3 months postoperatively. (C) Six years and 4 months postoperatively.

FIG. 5

(A) Age 7 years. (B) Three months postoperatively showing absorption of bone around screw and medial graft.

FIG. 6

(Same case as Fig. 5.) (A) Recurrence of pseudarthrosis 23 months postoperatively. (B) Seven months postoperative second graft.

previously a single onlay graft had been used. The other children are wearing braces and have been weight bearing for 14 to 79 months. In all the bones have solidly united except in the most recent one who is now in a brace.

We believe that this method has certain advantages:

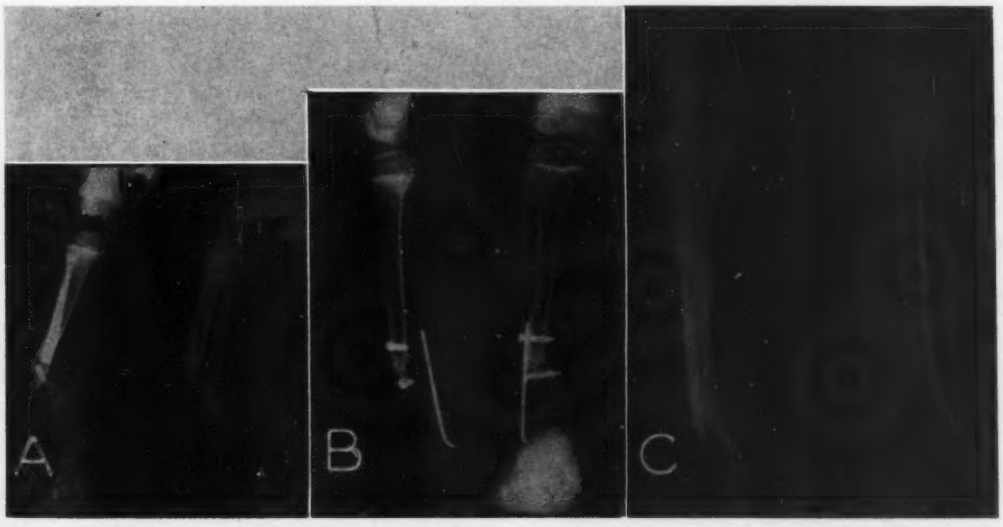
1. The two stage procedure permits complete excision of dense avascular fibrous tissue at the pseudarthrosis and correction of alignment retaining maximal length. A vascular receptive bed is thereby provided when the second stage is performed 6 to 8 weeks later.

2. The accessory fixation of the fibula apparently reinforces the immobilization but does not interfere with growth of the fibula.

3. Autogenous bone is used and is obtainable at an age as early as 4 years.

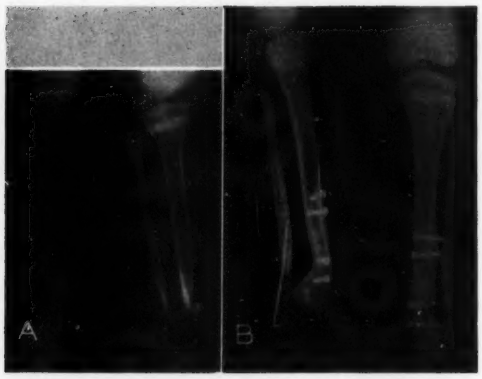
The problem of equalization of the length of the legs is still a difficult one. Its solution is being attempted by epiphysial arrest of the opposite tibia and fibula and sometimes the femur, performed when properly indicated. We have found too that most of these patients develop some calcaneous deformity. One who

FIG. 7



(A) Age 2 years. (B) Three years and 7 months after dual graft. (C) Four years postoperative grafting.

FIG. 8



(A) Age 7 years, 8 months. (B) One year postoperative graft.

was lost from follow-up for a time developed a valgus deformity of the ankle from a worn brace.

Summary

Variations in technic of dual bone grafting for pseudarthrosis of the tibia have been presented.

This technic offers what appears to be a better prognosis for union with a method which can be used early enough to decrease the tendency for shortening and calcaneous deformity.

FIG. 9

Age 4 years, 4 months, recent case.

Nine bone graft procedures have been performed on 7 patients with union obtained in each instance.

We intend to observe these patients closely and hope to present a 10 year follow-up on them subsequently.

Acknowledgment

These patients were all seen under the auspices of the Mississippi Crippled Children Service and the treatment of all of them by one of us was made possible by the generous assignment of all such cases on the service to that surgeon by the other orthopedists on the panel.

References

1. Boyd, H. B.: Congenital Pseudarthrosis. Treatment by Dual Bone Grafts, J. Bone & Joint Surg. 23:497, 1941.
2. Boyd, H. B., and Fox, K. W.: Congenital Pseudarthrosis. Follow-up Study After Massive Bone Grafting, J. Bone & Joint Surg. 30-A:284, 1948.
3. Moore, J. R.: Delayed Autogenous Bone Graft in the Treatment of Congenital Pseudarthrosis, J. Bone & Joint Surg. 31-A:23, 1949.
4. Kite, J. H.: Congenital Pseudarthrosis of Tibia and Fibula, South. M. J. 34:1021, 1941.
5. Boyd, H. B., and Sage, F. P.: Congenital Pseudarthrosis of the Tibia, J. Bone & Joint Surg. 40-A:1245, 1958.

Discussion (Abstract)

Dr. J. Hiram Kite, Atlanta, Ga. There is some unknown factor in congenital pseudarthrosis which prevents the growth of bone. In the lower third of the tibia and fibula in these cases there is an area of imperfect osteogenesis. The bone does not appear normal in the roentgenogram before the fracture, and after the fracture there is no callus formation. When bone grafts are applied, there is still no callus formation, and often there is a surprising rapid absorption of the grafts. When the grafts do take and union has occurred, there is very little increase in the thickness of the shaft. If the medullary canal is restored shortly after the operation, it may gradually be obliterated by the formation of sclerosis at the site of the original fracture. The grafted area gradually bends, even when protected by as good bracing as it is possible to apply. Before long the bone yields to the strain, and an insufficiency fracture develops; the leg may fracture from a very slight injury, even while wearing the brace.

In 1940, I read a paper before this same group, and reported 15 cases of congenital pseudarthrosis of the tibia or fibula, or both. I now have had 23 of these cases collected over 35 years; 4 of the clavicle, and one of the ulna. The cases early in my series were treated by various technics of bone grafting as used at that time. Many nonunions followed our attempts at bone grafting. One day, Dr. Lawson Thornton operated upon a patient in whom he raised a bone flap from the side of the tibia above and below the fracture site, and slipped a bone graft under the flaps, and let the elasticity of the flaps hold the graft in place. This tibia united. We continued to use the end-under-bone-flap method with one graft, until Harold Boyd suggested the dual graft. Since then we have used two grafts by the same method. If the flap breaks, we use a screw. We have always used autogenous grafts.

Drs. Purvis and Holder insert a wire in the fibula

when it is fractured to give better internal fixation. In some of our cases the fibula was not fractured, and yet the graft failed to produce union in the tibia. They say that the two stage operation provides a vascular receptive bed for the graft. John Royal Moore used a delayed bone graft and fixed the fibula with a Kirschner wire in his report in 1948. The two stage operation can be carried out more readily on charity patients than on private patients because of the expense. The dual graft recommended by Boyd seems to me to be the most important step in the operation.

The authors obtained nine unions in nine operations which is excellent. It is perfect. I have had many disappointments following my bone grafting in these cases, especially those done 30 years ago.

In doing a bone graft for nonunion in an ordinary fracture in normal bone, we expect the limb to be restored to normal appearance and function. This is not true in congenital pseudarthrosis. Even if we get union we have a very imperfect leg. An unsightly brace has to be worn until growth is almost complete, and even then these legs fracture easily if subjected to much strain. One of their patients discarded her brace at 16 years, but all the others are in braces. Three of my patients with solid union demanded amputation in their teen age, rather than continue to wear the brace. If the union becomes solid enough to leave off the brace, there is shortening up to as much as six inches, in a few cases. This requires an ugly lift or a brace. Often a deformity of the foot adds to the bad appearance of the prosthesis.

Obtaining union in this difficult condition is a surgical triumph, but it falls short of giving the child the good leg the parents expected. In some of these patients it is a difficult question to decide between doing a bone graft operation or an amputation. If the foot is deformed and there is already considerable shortening, an amputation might be the procedure of choice.

EDITORIAL

THE GENERAL HOSPITAL AND THE CARE OF THE MENTALLY ILL

A recent editorial on these pages pointed to the efforts of the American Academy of General Practice and the American Psychiatric Association to develop a postgraduate program which would develop an interest in, and sufficient psychiatric technic to engage the general practitioner in the management at least of some of the less severe degrees of mental illness.[1] There is a great need for such interest and instruction for several reasons. In the first place, the increase in the number of psychiatrists has lagged far behind the advances in psychiatric management and the expanding recognition of the need of their help by both patients and their doctors. (It is certain that many years will elapse before the need and supply will be matched.) The family and industrial physician stand in a position where they can practice preventive psychiatry, with their intimate knowledge of the patient and his place in the family circle or in his environment. Also, in the lesser mental disturbances they may quite quickly aid the patient to find his way out of the problems which may have engulfed him for the moment. The disturbances which are more deeply rooted will probably continue to need the specialized care of the trained psychiatrist.

Another and somewhat startling concept is showing rapid growth. This is the thought that the general hospital should admit psychiatric patients for care of the "acute" and the lesser mental disturbances. This will need a re-orientation of both hospital staffs and administration. Koltes and Matthews[2] have emphasized the rapidly changing acceptance of such a viewpoint. At the turn of the century about 25 of the general hospitals of the country had a psychiatric service. There was gradual increase until after World War II, when there were 200 such services (in 1945). Since then the increase of psychiatric services has multiplied so rapidly that by 1957 there were 584 in the country, with new ones being opened at this increased rate.

In the main, the state mental hospitals were conceived of as offering humane custodial care and have continued as such even to the present time, in fewer and fewer instances. In the earlier years of the twentieth century psychiatry as a medical science was slowly growing to gain recognition and expansion; a great impetus came with the catastrophies of World War I. With this stimulation, and the development of reasonably satisfactory treatment for the organic disease general paresis, and the introduction of shock therapy for certain functional psychoses, psychiatry made rapid strides. Psychotherapy for the mentally ill was also moving forward.

World War II advanced the role of psychiatry even more. Now came new understanding of both the major and lesser psychoses and a knowledge of the numbers of maladjusted persons in the population. The application of psychologic testing and electroencephalography assumed important roles in the study and diagnosis of mental disease. Lastly, but by no means the least, came the development of the ataractic drugs for the treatment especially of the disturbed patient. The rapidity with which these patients are controlled and made accessible to psychotherapy is nothing short of amazing, as compared to the weeks and weeks of observation and care needed in past years for such improvement.

With these advances the state mental institutions have taken on an increasing role as treatment centers at the expense of custodial care. Doors are being unlocked to permit patients a more normal freedom of movement. Recreational and occupational activities are increasing, and more and more patients are being discharged to their homes and communities.

Anyone who thinks upon these historical advances in psychiatry anticipates yet another change, the admission of the acutely disturbed

1. Bedell, Sullivan G.: Editorial—The General Practitioner and Psychiatry, South. M. J. 53:379, 1960.
2. Koltes, John A., and Matthews, Robert A.: Editorial—Mental Illness and the General Hospital, Am. Pract. & Digest. Treat. 11:263, 1960.

patient or one with lesser psychiatric problems to the general hospital. Here he may be brought under control quickly with drugs and/or psychotherapy, without the psychologic hazard of having been committed to a mental institution. (In some general hospitals the psychiatric division is "open," in others "closed." This will need to be an individual development.) Every general hospital admitting psychiatric patients under these circumstances must have well-trained psychiatric consultants.

The final point to be made for psychiatric admissions to a general hospital, in addition to the lessened psychic trauma for the patient and his family, is the educational and training value. Heretofore, the psychiatrist generally has been isolated from his professional confreres to the detriment of both himself, to others of the profession and to the patient. The isolation of both the patient and his doctor in a mental hospital has deprived the patient of easily facilitated consultation on occasion, and inhibited professional intercourse among the doctors of the community. Admission of the mentally ill to a general hospital would do away with these hurdles. And returning to the need for educating and training the family doctor to his place in the practice of psychiatry, it can be done best in the surroundings of the general hospital. Here his patient can be seen in consultation with the consulting psychiatrist and the course of psychotherapy be outlined for management after the patient's discharge,—this is learning by doing under instruction and observation. The house staff will learn by precept and observation these same things so they will be equipped to engage in some degree of psychiatric practice upon completing their graduate training.

The opening of the general hospital, therefore, is a foregone conclusion. When, will depend upon the individual hospital and the community. The forward-looking reader of this page may be the catalyst who will advance the welfare of the patients in his area by providing for them potential total care within the resources of his medical community.

25 YEARS AGO

Pneumonias Due to Pneumococcus Type VIII.*

"With the introduction of type specific therapeutic sera it has become desirable to classify the pneumonococcus pneumonias in accordance with the etiologic type and, if possible, to differentiate them clinically.

"The separation of the pneumonococci into specific types ultimately depends on the production of type specific antibodies as the result of their reaction with certain animal hosts. . . .

"Specific differences due to the pneumococcus may exist in respect to invasion, course, symptoms and physical signs. It is our purpose to describe the reactions of the body to Pneumococcus Type VIII. Our studies only permit us to sketch the disease picture; details must await more extended observations. At first many cases of Type VIII were included with Type III and unless care is taken they may still be thus designated. . . .

"We base our description chiefly on 122 cases in adults (constituting 5.9% of 2,067 pneumonococcus pneumonias) and 11 cases in children (constituting 2.2% of 500 pneumococcus pneumonias studied on the Pediatric Service. . . . The cases were observed during a 5-year period, July 1, 1928, to June 30, 1933. Since then we have observed more than 60 cases among adults on our Adult Service, a few on the Children's Service and several in private practice. The number of admissions to our service due to this disease has increased in recent years. This is not due to a transfer of cases from Type III to Type VIII because of more precise bacteriological work. . . .

"*The Disease as Seen in Man.* There are as yet no physical criteria by means of which one can postulate with great probability that a patient who is suffering from pneumonia is infected with Pneumococcus Type VIII.

". . . In our cases the onset occurred with a head or chest cold in 23% of the cases, with a chill or chilly sensations in 75% and with pain in the chest in 89%. These symptoms were not especially severe.

"We have observed that Type VIII pneumonia patients do not, as a rule, appear very acutely ill at first. Clinicians with sufficient experience might well question a report of Type III from a patient who is not severely prostrated and request verification of the type from additional studies and fresh specimens of sputum. . . .

*Bullowa, J. G. M.: Pneumonias Due to Pneumococcus Type VIII, Am. J. M. Sc. 190:65, 1935.

". . . The relative frequency of severe, mild and moderate cases in Types VIII and III, and the mortality in severe cases, are contrasted in Graph 2. Among the Type III pneumonias there were more severe cases (42%) than there were among the Type VIII pneumonias (26%). More mild cases occurred among the Type VIII cases (47%) than among those due to Type III (15%). The severe cases were more numerous among the Type III pneumonias (42%) than among those caused by Pneumococcus Type VIII (15%). Many more of the severe Type III cases (78%) died than the severe Type VIII cases (45%). Temperature always below 102°F. was observed in 5% of the Type VIII cases, and pulse below 110 was observed in 11%. . . .

"Diarrhea, pulmonary edema and dehydration are seen to be of serious omen. Apparently the occurrence of a positive Kahn reaction was unimportant. It is significant that 40% of the Type VIII bacteremias occurred in mild and moderate cases. The recovery of a patient whose blood was invaded by Pneumococcus Type III was extremely rare.

"Termination. Among the 105 cases who recovered, 32 (30.1%) terminated by crisis and 74 (69.8%) ended by lysis.

"The physical signs may be quite classic and well defined, involving an entire lobe. On the other hand there are many more cases in which an entire lobe is not consolidated or the consolidation becomes manifest more slowly. There may be only slight dullness, or breathing is distant and the tubular characters are pronounced. . . .

"Bloody or rusty sputum is encountered in pneumonia cases produced by Pneumococcus Type VIII. . . . In the presence of consolidation and hemoptysis we must suspect, in addition to pulmonary tuberculosis, pneumonia due to either B. Friedlander or Pneumococcus Type III or Type VIII. Pneumonia due to B. Friedlander is relatively infrequent 1%, whereas pneumococcus pneumonia due to Type VIII or Type III, in the period from 1928 to 1934, constituted 22.2% of all pneumonococcus pneumonias. . . .

"Bacteremia. One of the features of pneumonia which seems to be characteristic of each type is the frequency and severity of bacteremia. Graph 8 shows the relatively low bacteremic incidence of Type III cases (12%) as contrasted with Type VIII (20%). In the non-serum cases the bacteremic mortality for Type VIII is 42%, and for Type III 100%. . . ."

SOUTHERN MEDICAL NEWS

State News Items

Dr. J. H. McCurry, Cash, Arkansas, is organizing a Fifty Year Club of American Medicine as a "social function to honor physicians who have been in the practice of medicine fifty years or more. . . ." This organization is to be completely independent of the AMA and self supporting. There will be no dues, but a fee of about $2.00 to pay for lapel buttons, Appreciation certificates, postage, etc. The first meeting will be held in Washington, D. C., at the AMA Clinical Meeting, around November 30. For further information write Dr. J. H. McCurry, Cash, Arkansas.

The tenth Biennial Southeastern States Cancer Seminar for Physicians will be held at the Cherry Plaza Hotel, Orlando, Florida, November 16-18, 1960. The theme "New Horizons of Cancer Research and Therapy" will feature 14 nationally prominent guest speakers. There is no registration fee. For advance reservations or additional information contact 1960 Cancer Seminar Committee, 17 Lake Street, Orlando, Florida.

The Laboratory Branch of the Communicable Disease Center, Atlanta, Georgia, has completed a schedule of Laboratory Refresher Training Courses which are to be offered October 10, 1960 to April 7, 1961. The first course, "Fundamentals of Virology," will be presented October 10-21, 1960. For a complete schedule and application forms write to the Laboratory Branch, Communicable Disease Center, U. S. Public Health Service, Atlanta 22, Georgia.

The American College of Gastroenterology announces that its Annual Course in Postgraduate Gastroenterology will be given at the Bellevue-Stratford Hotel in Philadelphia, Pennsylvania, October 27-29, 1960. The Course will cover the advances in diagnosis and treatment of gastrointestinal diseases and a comprehensive discussion of diseases of the mouth, esophagus, stomach, pancreas, spleen, liver and gall bladder, colon and rectum. For more details write to the American College of Gastroenterology, 33 West 60th Street, New York 23, New York.

The University of Colorado School of Medicine, Department of Pediatrics, and the Office of Postgraduate Medical Education of the University of Colorado Medical Center will offer a postgraduate course in Pediatrics, September 1-6, 1960, at the Stanley Hotel in Estes Park, Colorado. The program will be divided into two parts: Clinical and Research Advances in Pediatrics (September 1-3), and Child Guidance (September 5 and 6). Physicians may register for the entire course or for either part. The tuition fee will be $60.00 for the entire program or $30.00 for either part. There is also a $10.00 registration fee which is non-refundable. For an application form contact the Office of Postgraduate Medical Education, University of Colorado Medical Center, 4200 East Ninth Avenue, Denver 20, Colorado.

ALABAMA

Dr. J. F. A. McManus, member of the Editorial Board of the *Southern Medical Journal* and Chairman

Continued on page 937

1. Mr. Robert F. Butts, left, Executive Secretary-Treasurer of Southern Medical Association, and Dr. J. Garber Galbraith, right, President of the Jefferson County Medical Society, also SMA Councilor from Alabama, present Mr. Edwin Steven Yates, center, Executive Secretary of JCMS, with an Associate Membership in SMA. 2. Mrs. John M. Chenault, center, Decatur, chats with Mrs. Frank Gastineau, left, Indianapolis, President of the Woman's Auxiliary to the American Medical Association, and Mrs. George W. Smith, right, Columbia, South Carolina, the new President of the Woman's Auxiliary to the South Carolina Medical Association. The women are pictured in front of the SMA exhibit at the annual meeting of the South Carolina Medical Association in Myrtle Beach, May 17-19. 3. Dr. Guy T. Vise, left, Meridian, SMA Councilor from Mississippi, presents Mrs. J. M. Hood, Sr., Houlka, with an Honorary Membership in SMA for her husband, Dr. J. M. Hood, Sr. Dr. Hood has been a member of SMA since 1922. Looking on is Mr. J. M. Hood, Jr., son of the honoree. This award was made at the annual session of the Mississippi State Medical Association, May 10-12, in Jackson. 4. Dr. Vise presents Dr. Harvey F. Garrison, Jackson, Mississippi, with a Certificate of Appreciation and an Honorary Membership in SMA for his services as a Section Officer, Councilor, President and Trustee. 5. Mr. Rowland B. Kennedy, left, Jackson, Executive Secretary of the Mississippi State Medical Association, receives an Associate Membership in SMA from Dr. Edwin H. Lawson, right, New Orleans, SMA President.

Know Your Southern Medical Association

The Employee Retirement Plan

After many years of study, and the setting aside of reserve funds, the Southern Medical Association established a retirement plan for its employees on November 30, 1954. The Plan, which is financed by an irrevocable trust, complies with the requirements of Section 401(a) of the Internal Revenue Code of 1954 respecting the establishment of such plans, and the earnings of the Trust are exempt from taxation under the provisions of Section 501(a) of said Code.

Employee's Pension Trust

The Trust fund was created by the deposit of an original corpus of $169,187.50 consisting of appropriated cash and bonds of the Association with the Trustee, the First National Bank of Birmingham. The corpus, now approaching $200,000.00, has been augmented by (1) earnings on investments of the Trust funds, and (2) periodic contributions from the Association which are actuarially determined as necessary to maintain the fund on a sound basis.

The nominal administrative expense of managing the Trust is paid out of current Association funds so that all of the earnings of and contributions to the Trust are added to the corpus.

The Trust fund is noncontributory on the part of employees; it being the purpose of the Association to fund the Trust through investments and periodic contributions. No employee has any vested interest in any of the assets of the Trust fund, and there are no severance or death benefits.

How the Trust is Administered

The Trust fund is administered by the Trustee, the First National Bank of Birmingham, pursuant to the provisions of a Trust Agreement. The Trustee collects and receives income for the fund, recommends investments, disburses payments to retired employees, and renders an annual financial statement of the condition of the fund to the Association. There are presently six persons receiving benefits from the Plan.

The Retirement Committee

While the financial management of the Trust is vested in the Trustee, the actual control of the Trust is exercised by a three man Retirement Committee of the Association. Among other duties, the Committee determines eligibility of employees for benefits, certifies the amounts payable, actuarially determined, to eligible beneficiaries, authorizes disbursements, approves the recommendations of the Trustee on investments, and maintains pertinent records of the operation of the Plan.

All Employees Eligible

All employees of the Association, except temporary employees, may become members of the Plan by executing a "Request for Membership" form and filing it with the Retirement Committee. Pertinent employment records on each employee are furnished the Committe by the Association.

Requirements for Benefits

To be eligible for benefits, an employee must:

(1) have reached the normal retirement age of 65 and completed at least 5 years of continuous service to the Association, or

(2) have become totally and permanently disabled while in the employ of the Association, or

(3) be within 10 years of normal retirement age (55 or more) with at least 15 years of continuous service to the Association.

Benefits Provided by the Plan

(1) Employees having reached the normal retirement age of 65 receive a monthly retirement income for life equal to one per cent (1%) of their monthly salary (averaged over the last 36 months of employment) for each

APPLICATION FOR HOTEL ACCOMMODATIONS

Southern Medical Association

Saint Louis, Missouri

October 31-November 3, 1960

IMPORTANT: The Convention Reservation Bureau will make hotel assignments upon receipt of this official housing application provided that the application is properly filled out and all necessary information is given. In order that a fair distribution of accommodations can be made to the greatest number of members, all rooms will be assigned on a strictly "first come, first served" basis.

INSTRUCTIONS: *(A) Single rooms are limited in number. Please arrange to occupy double bedded or twin bedrooms if possible. No block reservations will be made.*

(B) Be sure to indicate your arrival time in St. Louis. Reservations will be held only until 6:00 p.m. of the day you indicate when you will arrive in St. Louis. Failure to notify the hotel of any last minute change in your arrival time may result in the cancellation of your reservation.

(C) Write the Convention Reservation Bureau, 911 Locust Street, St. Louis, if you wish to cancel the reservation or make any change in your reservation and NOT the hotel to which you were assigned. This will enable them to reassign rooms that have been cancelled.

(D) If the hotels of your choice are unable to accept your reservation, the Convention Reservation Bureau will make as good a reservation as possible elsewhere provided that all hotel rooms available have not already been taken.

Hotel	For one person	For two persons		2-Room Suite Parlor & 1 Bedroom
		Double Bed	Twin Beds	
CLARIDGE	$5.50-$ 8.00	$ 8.00-$10.00	$10.00-$14.00	$16.00-$18.00
DESOTO	5.50- 8.50	7.00- 10.00	8.50- 12.00	17.50
LENNOX	7.50- 13.00	9.00- 14.00	13.00- 13.50	20.50- 35.00
MAYFAIR	7.50- 13.00	9.00- 14.00	13.00- 14.00	21.00- 35.00
PICK-MARK TWAIN	6.50- 9.00	8.50- 11.50	10.00- 12.50	17.50- 27.00
SHERATON-JEFFERSON	8.50- 11.00	12.00- 14.50	13.85- 18.00	28.00- 49.00
STATLER-HILTON	8.00- 11.50	11.00- 14.50	13.00 -15.00	29.50- 36.50
WARWICK	5.50- 8.00	8.50- 12.00	9.50- 12.00	

CONVENTION RESERVATION BUREAU
SOUTHERN MEDICAL ASSOCIATION
911 Locust Street, Room 406
Saint Louis 1, Missouri

Please reserve the following accommodations for the Southern Medical Association Meeting, October 31-November 3, 1960:

Hotel Preference	Kind of Accommodations Desired
1st Choice.....	.....Single room at $.....to $.....
2nd Choice.....	.....Double room at $.....to $.....
3rd Choice.....	.....Twin bedroom at $.....to $.....
	.....2-Room Suite at $.....to $.....
	.....Other type .....

Arrival Date.....hour.....a.m.....p.m.

Departure Date.....hour.....a.m.....p.m.

THE NAME OF EACH HOTEL GUEST MUST BE LISTED. Reservations cannot be made in any hotel unless two names are given for each double bedded room or twin bedded room. If this information is not given on your original application, the Convention Reservation Bureau must send you a card asking that you submit two names. This means unnecessary delay and lessens the possibility of assignment to the hotel of your choice.

Name of Occupant (s) (Please type or print)	Address
.....	.....
.....	.....
.....	.....

Individual Requesting Reservations
(Please type or print)

NAME.....

ADDRESS.....

CITY.....ZONE.....STATE.....

From:

_____

_____

_____

PLACE
STAMP
HERE

CONVENTION RESERVATION BUREAU

Southern Medical Association

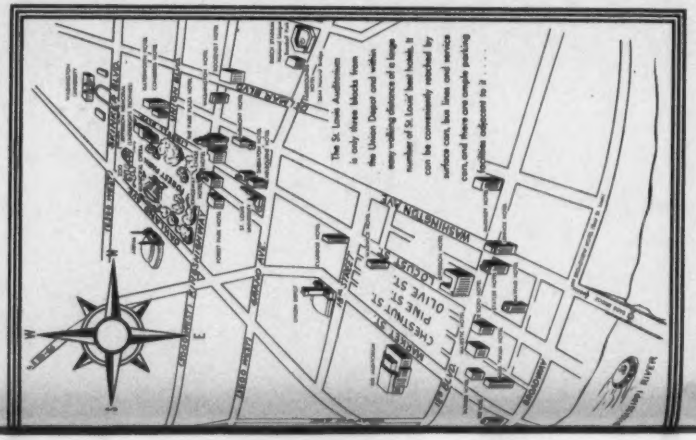
911 Locust Street, Room 406

Saint Louis 1, Missouri

FIRST FOLD HERE

SECOND FOLD HERE

THIRD FOLD HERE


The St. Louis Auditorium is only three blocks from the Union Depot and within easy walking distance of a large number of St. Louis' best hotels. It can be conveniently reached by surface cars, bus lines and service cars, and there are ample parking facilities adjacent to it.
WASHINGTON AVE.
LOCUST ST.
CHESTNUT ST.
PINE ST.
OLIVE ST.
MARKET ST.
MISSISSIPPI RIVER

full year of continuous service. However, no monthly retirement income shall be less than thirty per cent (30%) of the retiring employee's income provided that the employee shall have had at least five years of continuous service.

(2) An employee who becomes totally and permanently disabled while in the employ of the Association will receive disability benefits equal to the amount provided by the actuarial value of that employee's reserve liability of the fund.

(3) An employee eligible for retirement, and who elects the joint-survivorship retirement income plan, will receive a reduced monthly income for life. The surviving spouse will then receive two thirds of said reduced income for life.

By mutual consent, an employee who has reached retirement age may remain in the active employment of the Association. Retirement benefits for such employee will not begin until the employee actually retires.

Amendments

Provision is made for amendments to the Plan and to the Trust Agreement, provided that no amendment shall have a retroactive adverse effect upon current members of the Plan.

Plan Intended to be Permanent

The Plan was established in good faith and on a sound actuarial basis with the intent that it would be perpetuated. However, the Plan is strictly voluntary, and the Association reserves the right to amend, modify, or discontinue the Plan if unforseen conditions warrant. In the event of a dissolution, the assets of the Trust must be distributed to retired employees and to eligible members on an equitable and actuarial basis, with the remainder, if any, reverting to the Association.

V. O. F.

MEDICAL NEWS

Continued from page 934

of the Department of Pathology of the University of Alabama Medical Center, has been elected as a Council member of the American Society for Experimental Pathology.

Dr. Henry C. Hudson, Birmingham, was elected Treasurer of the Southeastern Section of the American Urological Association.

Officers of the Birmingham Society of Internists include Dr. Charles Crow, President; Dr. Richard Carter, Vice-President; Dr. Stanley Kahn, Secretary-Treasurer; and Drs. Joe Reeves, Al Shugerman, Hampton Smith, Stephen Stigler and Joe Weldon, Executive Committee members.

New members of the Jefferson County Medical Society are Drs. Glenn D. Barnes, Chester C. Brummett, Charles E. Butterworth, Floyd O. Fitts, Jr., Charles M. Johnson, and Gilder L. Wideman, all of Birmingham.

ARKANSAS

Officers of the Lawrence County Medical Association include Dr. Ralph Joseph, President; Dr. Jerry Whittington, Vice-President; Dr. Lloyd Gregory, Secretary-Treasurer; and Dr. J. B. Elders, Delegate, all of Walnut Ridge.

Dr. Lonnie Turney, McGehee, is President of the Southwest Arkansas Medical Society.

Drs. Thomas M. Ferguson, West Memphis, and Robert F. McCrary, Hot Springs, have been certified in gynecology by the American Board of Obstetrics and Gynecology.

DISTRICT OF COLUMBIA

Dr. Paul B. Cornely has been elected to a 3 year term on the Board of Trustees of Davis Memorial Good Will Industries.

Dr. Stanhope Bayne-Jones has been awarded the honorary degree of Doctor of Laws from the Johns Hopkins University.

Dr. Lawrence E. Putnam has been appointed Editor-in-Chief of two medical journals, *Antibiotic Medicine & Clinical Therapy* and *Antibiotics & Chemotherapy*. Dr. Putnam is Assistant Clinical Professor of Medicine at George Washington University School of Medicine and is on the hospital staffs of four D. C. hospitals.

Dr. Laurence H. Kyle, Professor of Medicine at Georgetown University School of Medicine, has been elected President of the Southern Society for Clinical Research.

Dr. Elbert T. Phelps, Assistant Professor of Medicine at Georgetown University School of Medicine, has been appointed Director of the Outpatient Department of the Hospital.

FLORIDA

The Greater Miami Society of Anesthesiologists has announced the following officers: Dr. Sanford Cobb, President; Dr. Hugh J. Forthman, Vice-President; and Dr. Edward A. Talmage, Secretary-Treasurer. Dr. Cobb has also recently been certified as a Diplomate of the American Board of Anesthesiology.

Dr. Carlos P. Lamar, Miami, gave the eighth annual B. B. Weinstein Lecture at the 33rd Annual Banquet of the Medical Historical Society of Tulane University on May 20. His subject was "Comments on the History of Diabetes." On May 22, Dr. Lamar spoke at Touro Infirmary in New Orleans on "New Concepts on Diabetology."

Captain Herbert H. Eighmy, MC, USN, has been assigned Commander of the U. S. Naval Hospital, Naval Aviation Medical Center in Pensacola.

Officers of the Florida Medical Association are Dr. Leo M. Wachtel, Jacksonville, President; Dr. H. Carnes Harvard, Brooksville, President-Elect; Dr. Clyde O. Anderson, St. Petersburg, Vice-President; and Dr. Sam Day, Jacksonville, Secretary-Treasurer.

Dr. Jerome A. Raim, Miami, and Dr. Henry F. LaGuette, Coral Gables, have been certified by the American Board of Urology.

Dr. Albert Jaslow, Miami, has been appointed senior physician for the Outpatient Clinic of the Florida Alcoholic Rehabilitation Program.

The following Florida physicians have been certified by the American Board of Obstetrics and Gynecology: Dr. Malcolm C. Crotzer, Ft. Walton Beach; Dr. Jack Fealy, West Palm Beach; Dr. Harold G. Foss, South Miami; Dr. J. C. Gilbert, Jr., Ft. Lauderdale; Dr. Caroline B. Hunter, Coral Gables; and Dr. Irving B. Lees, West Palm Beach.

GEORGIA

Dr. Jack C. Norris, Atlanta, Second Vice-President of Southern Medical Association, has been presented a certificate of appreciation for his outstanding service as a member of the Blood Service Committee, Greater Atlanta Chapter, American Red Cross.

Officers of the medical staff of Gordon County Hospital are Dr. J. LeRoy Rabb, Calhoun, Chief; Dr. Charles K. Richards, Calhoun, Vice-Chief; and Dr. Byron H. Steele, Fairmount, Secretary.

Dr. James A. Redfearn, Jr., is President of the Hamilton Memorial Hospital medical staff. Dr. A. M. Boozer is Vice-President and Dr. D. M. Nowell is Secretary, all of Dalton.

Dr. Webster A. Sherrer, Marietta, has passed his examinations in Clinical Pathology for certification by the American Board of Pathology.

Dr. Ivey Jacobs, Waycross, has been admitted to the Holstein-Friesan Association, one of the world's largest dairy cattle registry organizations.

The Fulton County Medical Society has elected the following officers: Dr. J. G. McDaniel, President-Elect; Dr. William Moore, Vice-President; and Dr. Thomas J. Anderson, Jr., Secretary-Treasurer. The doctors are all from Atlanta.

KENTUCKY

Dr. J. Murray Kinsman, Dean of the University of Louisville School of Medicine, is First Vice-President of the American College of Physicians.

Officers of the Kentucky Industrial Medical Association include Dr. Eugene H. Kremer, Louisville, President; and Dr. Charles Martin, Lexington, President-Elect.

Governor Bert Combs has appointed Dr. W. Gerald Edds, Calhoun, to the Board of Regents of Western Kentucky College and Dr. R. W. Bushart, Fulton, to the Board of Trustees of the University of Kentucky. Governor Combs also appointed Dr. Boyce E. Jones, London, to the Kentucky Tuberculosis Hospital Commission.

Dr. Harold D. Rosenbaum, Lexington, has been named Chairman of the Department of Radiology at the University of Kentucky's College of Medicine.

LOUISIANA

Officers of The New Orleans Graduate Medical Assembly include: Dr. Maurice E. St. Martin, President; Dr. Barrett Kennedy, President-Elect; Dr. Ralph M. Hartwell, First Vice-President; Dr. Boni J. DeLaureal, Second Vice-President; Dr. J. Theo Brierre, Third Vice-President; Dr. Mannie D. Paine, Jr., Secretary; Dr. Max M. Hattaway, Treasurer, also Southern Medical Association Councilor from Louisiana; Dr. W. E. Kittredge, Director of Program; and Drs. Walter F. Becker and Daniel W. Hayes, Assistant Directors of Program. Members of the Executive Committee are Drs. Ambrose H. Storck, Richard L. Buck, Lee D. McLean, John G. Menville, and Daniel C. Riordan, also Chairman of the Section on Orthopedic and Traumatic Surgery for SMA. The twenty-fourth annual meeting of the Assembly will be held March 6-9, 1961.

The Ochsner Clinic in New Orleans has announced the appointment of Dr. Merrill O. Hines as Medical Director and the retirement of Dr. Guy A. Caldwell from the position. Dr. Caldwell, a founding partner of the Clinic, will continue to serve as a Trustee and Vice-President of the Alton Ochsner Medical Foundation.

MARYLAND

Officers of the Arlington County Medical Society are Dr. Michael A. Puzak, President-Elect; Dr. Sigmund Newman, Vice-President; Dr. Howard O. Mott, Secretary; and Dr. Robert B. Neu, Treasurer.

Dr. John S. Haught, Mt. Rainier, is President of the Prince Georges County Medical Society. Other officers include Dr. Ronald S. Fleischer, Hyattsville, Vice-President; Dr. Albert Roth, Riverdale, Secretary; and Dr. Norman D. Comeau, Mt. Rainier, Treasurer.

Dr. Edwin N. Broyles, Baltimore, is President of the American Laryngological Association.

Dr. Georgeanna S. Jones, Baltimore, is Honorary Vice-President of the American Society for the Study of Sterility.

MISSOURI

Dr. Axel N. Arneson, St. Louis, is Treasurer of the American College of Obstetricians and Gynecologists.

The following Missouri physicians have recently been certified by the American Board of Obstetrics and Gynecology: Dr. Robert A. Brennan, St. Louis; Dr. Ira C. Gall, St. Louis; Dr. Walter A. German, Jr., Springfield; and Dr. James S. Johnson, Kansas City.

Dr. Oscar Hampton is President of the St. Louis Orthopedic Society. Other officers are Dr. Ralph K. Earp, Vice-President, and Dr. Richard E. Lord, Secretary-Treasurer. The physicians are all of St. Louis.

Dr. Thomas J. Cooper, St. Louis, has been elected Councilor of the State of Missouri Society of Clinical Pathology.

NORTH CAROLINA

Dr. Kenneth M. Brinkhous, Professor and Chairman of the Pathology Department at the University of North Carolina School of Medicine, has been presented the Professor Award given annually by the

senior class to the faculty member "who by his willingness, understanding, and ability has contributed most to our medical education." Dr. Henry L. Stephenson was presented the Henry C. Fordham Award.

Dr. Nathan A. Womack, Head of the Department of Surgery at the University of North Carolina School of Medicine, has been elected President of the National Board of Medical Examiners, and President of the United Medical Research Foundation.

Dr. George P. Vennart has been appointed as Associate Professor of Pathology in the School of Medicine at U. N. C.

Dr. Thomas D. Kinney has been named Professor and Chairman of the Pathology Department at the Duke University Medical Center.

Newly-elected to fellowship in the New York Academy of Sciences is Dr. Philip Handler, Duke University School of Medicine.

OKLAHOMA

Officers of the Oklahoma State Medical Association are Dr. Walter E. Brown, Tulsa, President; Dr. Clinton Gallaher, Shawnee, President-Elect; Dr. J. Hoyle Carlock, Ardmore, Vice-President; and Dr. Mark R. Johnson, Oklahoma City, Secretary-Treasurer.

Continued on page 54

BOOK REVIEWS

Diseases of Medical Progress

By Robert H. Moser, M.D., Associate Professor of Internal Medicine, Graduate School, Baylor University. 116 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1959. Price $4.75.

The author of this small volume has done an inordinate service to the medical profession in pointing up iatrogenic disease and the great amount of illness we as physicians produce in our patients. The reviewer has for a number of years pointed out to his students that the drugs which we have had made available to us in the past 20 to 25 years have a potency which we older physicians had never encountered in the drugs available for our use before 1930. With the introduction of sulfonamides and the pharmaceutical preparations subsequently, the doctor's armamentarium has been expanded beyond anything which could have been imagined. The potency of many of these drugs is so great, when measured in disturbance of physiologic and biochemical processes, that it is a foregone conclusion they should derange these processes of the body, all too often beyond what had been expected by the attending physician when he prescribed these drugs. The physician's daily problem is the balancing of the good of the potent drugs against the untoward side effects.

Dr. Moser has made a remarkable contribution to the physician in practice, if he will but read about and become aware of these untoward side effects.

The reviewer would agree with Dr. F. Dennette Adams of Boston, who wrote the foreword and said ". . . One would like to think that it would find its way to the desk of every physician and that each will study the pertinent section before initiating, in any of his patients, a therapeutic measure of whose dangerous potentialities he may not be fully aware."

Neoplastic Disease at Various Sites. Vol. I. Carcinoma of the Lung

Edited by J. R. Bignall, M.D., M.R.C.P., Assistant Physician, Brompton Hospital. 292 pages. Baltimore: Williams & Wilkins Company, 1958. Price $10.50.

The stated intention of this series, to present a detailed clinical picture of neoplastic disease, its pathology, natural history and treatment, has been expertly accomplished in this volume on carcinoma of the lung. The discussion properly begins with a detailed, lucid consideration of the statistics indicating the increasing incidence and causal association with smoking. The graphs in this section aid immensely, and the quiet use of color makes these the best yet seen by the reviewer. The pathology, course and therapy are next

INSTRUCTIONS TO CONTRIBUTORS

Exclusive Publication: Articles offered for publication must be contributed solely to the Southern Medical Journal.

Manuscripts: Manuscripts should be original copy, typewritten, double-spaced, with wide margins. Because of lack of space, it is necessary to limit the number of bibliographic references to twenty. Footnotes and references should conform to the following style:

1. Doe, J. E.: What You Should Know about It, South. M. J. 50:711, 1950.

Illustrations: Black and white glossy prints, preferably 5 by 7 inches, and drawings in India ink on white paper are required. The author's name, number and indication of top, if doubtful, should be attached. Necessary plates not exceeding six, or one and a half pages, will be furnished by the Journal.

Reprints: Reprints are available at publisher's cost. An order form will accompany author's galley proof and should be returned with the galley to the Editor.

Book Reviews: Books and monographs submitted for review should be mailed to the Editor. Acknowledgment will appear in the Journal. Selection rights reserved.

Editorial Address: All manuscripts, corrected galley proof, reprint orders, books for review and related correspondence should be addressed to the Editor, R. H. Kampmeier, M.D., Vanderbilt University School of Medicine, Nashville 5, Tennessee.

Business Address: All correspondence related to membership, subscriptions, advertising, and other business should be addressed to the Southern Medical Association, 2601 Highland Avenue, Birmingham 5, Alabama.

taken up in order each based on significant numbers of cases in the Brompton and Royal Marsden Hospitals series, closely observed and followed. The most impressive thing about this entire presentation is the cautious, reasoned attitude about every point of view that is adopted. The role of surgery is carefully shown to be restricted; the section on radiation is careful to point out the value of palliative surgical resection. Clinical-pathological correlations are drawn, but go no further than are warranted. Unusual presenting syndromes are outlined in a separate chapter, whose only omission is that of hypercalcemia.

The bibliography is complete, references being well interdigitated within the text to the American, as well as the British, literature. This book is unreservedly recommended for all who deal with chest disease in the adult.

Current Medical References

Edited by Paul J. Sanazaro, M.D., Associate Professor of Medicine, University of California School of Medicine. 504 pages. Los Altos, Calif.: Lange Medical Publications, 1959. Price $3.50.

The author of this pocket-sized reference book had a good idea when he organized a group of men representing several interests in medicine in sifting out pertinent articles which have appeared within the last two decades and setting forth current concepts and knowledge relative to the selected topics. The publication of this reference book presupposes that it will be revised periodically and at short intervals to keep the references "current." The great value of this reference book is that here the physician may find listed hundreds of papers with anywhere from one to a dozen references under a given disease entity. One can see immediately the boon of such a reference book to the house officer or to the medical student, who wishes to go to the library and read something recent and good on the disease with which a patient has just been admitted to the ward.

To the practicing physician who has limited library facilities, but whose own office, or the library of his hospital, or local medical society has a limited variety of journals, it offers signposts for investigation of the literature at hand. The reviewer believes that Dr. Sanazaro is to be complimented for a good idea, for its implementation and hopes that the reference list will be kept "current."

Encyclopedia of Medical Syndromes

By Robert H. Durham, M.D., Physician-in-Charge, Division of General Medicine, Henry Ford Hospital, Detroit. 613 pages. New York: Paul B. Hoeber, Inc., 1960. Price $13.50.

The author had a wonderful idea when he undertook to describe briefly almost 1,000 syndromes as described in this text. It offers to the medical writer, to the physician having interest in the history of medicine, and to the teacher a wealth of reference material without the need for time-consuming research. To the young physician and medical student the book should be fascinating, because it indicates so well the far-reaching results of making astute clinical observations and recording them. After all, most of the syndromes were described as a result of some doctor's careful observations, which were recorded. Fundamental research relative to these observations and correlated scientific explanations came much later, if at all, to account for the clinical observations. The *Encyclopedia* gives the pertinent references for the reader who wishes to investigate the descriptions in detail. The reviewer feels safe in saying that any physician who is really interested in medicine and keeps abreast of medical literature will get his money's worth in this book.

Physiology of the Eye. Clinical Application

By Francis Heed Adler, M.D., Professor of Ophthalmology, University of Pennsylvania School of Medicine, Philadelphia. Third edition. 780 pages. St. Louis: C. V. Mosby Company, 1959. Price $16.00.

Previous editions projected this textbook of ocular physiology to become the outstanding authoritative publication in this field. As the author candidly states, research in the last five years in several directions has changed the concepts previously held to be true. He was forced to rewrite many of the chapters. Those dealing with aqueous humor and intraocular pressure were drastically altered. He has been able to maintain his original preface of supplying basic knowledge of physiology and correlating it clinically. An updating of one's library by having this text available is recommended.

Sensitivity Reactions to Drugs

By M. L. Rosenheim, and R. Moulton, University College Hospital Medical School, London. 237 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1958. Price $7.00.

The edited proceedings of a symposium held in July 1957, organized by The Council for International Organizations of Medical Sciences (UNESCO and WHO), appear in a text consisting of 17 papers by such authorities as Ackroyd, Rich, Garrod, Moeschlin and Chase, interspersed with discussions. The introduction sets forth a classification of drug reactions, clearly separating idiosyncrasy, intolerance, overdosage, secondary and side effects from hypersensitivity-allergic reactions.

The largest number of papers (7) encompass hematologic sensitivity reactions. Those on drug thrombocytopenia and agranulocytosis are complete and excellent. Shorter, good papers on anticonvulsant megaloblastic anemia and chloramphenicol aplasia were included for completeness and stimulation presumably, since their modes of action have not been delineated.

The last three papers in this volume are worth reading to the last word, dealing with tissue reactions produced by sensitivity to drugs, the occurrence of collagen and connective tissue-type diseases as a manifestation of drug sensitivity, and arteritis due to drugs. The paper on antibodies to drugs by Dr. Chase is a good summary of sound investigation.

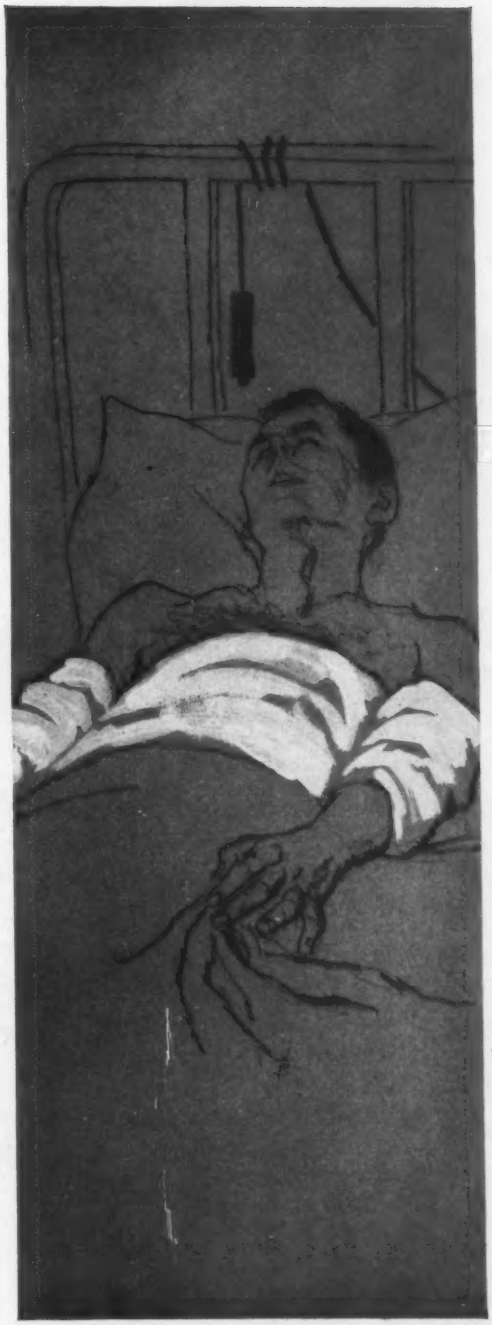
As must occur with multiple authorship, some papers seem weak by comparison, and others are outright flimsy.* The symposium as a whole represents excellent coverage of the field by authorities from various countries, and the chapters on tissue sensitivity are enthusiastically recommended.

*There is little clinical material, the accent being on a review of specific or postulated mechanisms.

In Acute Illness...

NILEVAR®

Can Speed Recovery



"Commonly, negative nitrogen balance[1] occurs during acute febrile illnesses and following traumatic events and surgical procedures." As much as 300 to 400 Gm. of nitrogen[2] may be destroyed daily in severe infections. Convalescence[1] is delayed when negative nitrogen balance is large and persistent.

NILEVAR Builds Protein, Speeds Convalescence to Complete Recovery[3-6] ". . . we were impressed[3] with the efficacy of Nilevar as an anabolic agent. All of the patients reported feeling much more vigorous and experiencing an increase in appetite. . . ."

The actions of Nilevar[4] in reversing a negative nitrogen balance—and therefore a negative protein balance—improving the appetite and increasing the sense of well-being can be expected to shorten the illness and the convalescence of these patients.

An initial daily dosage of 30 mg. of Nilevar (brand of norethandrolone) is suggested. After one to two weeks, this dosage may be reduced to 10 or 20 mg. daily in accordance with the response of the patient. Continuous courses of therapy should not exceed three months, but may be repeated after rest periods of one month. Nilevar is supplied as tablets of 10 mg., drops of 0.25 mg. per drop and ampuls of 25 mg. in 1 cc. of sesame oil with benzyl alcohol.

1. Eisen, H. N., and Tabachnick, M.: Protein Metabolism, M. Clin. North America 39:863 (May) 1955. 2. Jamison, R. M.: General Nutritive Deficiency, Virginia M. Month. 83:67 (Feb.) 1956. 3. Goldfarb, A. F.; Napp, E. E.; Stone, M. L.; Zuckerman, M. B., and Simon, J.: The Anabolic Effects of Norethandrolone, a 19-Nortestosterone Derivative, Obst. & Gynec. 11:454 (April) 1958. 4. Batson, R.: Investigator's Report, Feb. 11, 1956. 5. Weston, R. E.; Isaacs, M. C.; Rosenblum, R.; Gibbons, D. M., and Grossman, J.: Metabolic Effects of an Anabolic Steroid, 17-Alpha-Ethyl-17-Hydroxy-Norandrostenone, in Human Subjects, J. Clin. Invest. 35:744 (June) 1956. 6. Brown, C. H.: The Treatment of Acute and Chronic Ulcerative Colitis, Am. Pract. & Digest Treat. 9:405 (March) 1958.

G. D. SEARLE & CO.
CHICAGO 80, ILLINOIS

Research in the Service of Medicine

new
an antihistamine
that is an antihistamine
-not a somnifacient

RAPID ACTING

drowsiness *(other side effects)* rare...relief prompt...toxicity low

Investigators cite this new antihistamine's lack of side effects, its speed of action and its excellent tolerance. Nineteen investigators have treated over 800 patients with ALLERCUR. In 297 recent cases, 91% were side-effect-free. ALLERCUR is supplied in bottles of 100 scored tablets, each containing 20 mg. Clemizole HCl. Average dose is 2 to 4 tablets daily.

when allergies occur

Rx ALLERCUR®

(Clemizole HCl)

New York 17, New York • Division, Chas. Pfizer & Co., Inc. • Science for the World's Well-Being

®Trademark, Schering, A. G., Berlin Bibliography available on request.

CLINICAL REMISSION IN A "PROBLEM" ARTHRITIC

In "escaping" rheumatoid arthritis. After gradually "escaping" the therapeutic effects of other steroids, a 52-year-old accountant with arthritis for five years was started on DECADRON, 1 mg./day. Ten months later, still on the same dosage of DECADRON, weight remains constant, she has lost no time from work, and has had no untoward effects. She is in clinical remission.*

How convenient b.i.d. alternate dosage schedule: the degree and extent of relief provided by DECADRON allows for b.i.d. maintenance dosage in many patients with so-called "chronic" conditions. Acute manifestations should first be brought under control with a t.i.d. or q.i.d. schedule.

Supplied: As 0.75 mg. and 0.5 mg. scored, pentagon-shaped tablets in bottles of 100. Also available as injection DECADRON Phosphate. Additional information on DECADRON is available to physicians on request. DECADRON is a trademark of Merck & Co., Inc.

*From a clinical investigator's report to Merck Sharp & Dohme.

Decadron®

Dexamethasone

TREATS MORE PATIENTS MORE EFFECTIVELY

MSD MERCK SHARP & DOHME • Division of Merck & Co., INC., West Point, Pa.

an original development of Roc

t of Roche research

NEW 5 mg and 10 mg

LIBRIUM

THE SUCCESSOR TO THE TRANQUILIZERS

successor in specificity: relieves anxiety, agitation and tension, and liberates the patient from destructive fears.

successor in safety: not encumbered by depression, lacks autonomic or extrapyramidal side effects.

successor in versatility: covers the entire meprobamate area of therapy plus a significant portion of the phenothiazine area plus the difficult middle ground between the two.

successor in effect: acts with remarkable promptness; preserves full mental acuity; produces a feeling of well-being, increased drive and a broadening of interest.

Consult literature for dosage instructions.

Published reports on Librium: 1. T. H. Harris, *Dis. Nerv. System*, *21*:(Suppl.), 3, 1960. 2. L. O. Randall, *ibid.*, p. 7. 3. J. M. Tobin, I. F. Bird and D. E. Boyle, *ibid.*, p. 11. 4. H. A. Bowes, *ibid.*, p. 20. 5. J. Kinross-Wright, I. M. Cohen and J. A. Knight, *ibid.*, p. 23. 6. H. H. Farb, *ibid.*, p. 27. 7. C. Breitner, *ibid.*, p. 31. 8. I. M. Cohen, Discussant, *ibid.*, p. 35. 9. G. A. Constant, *ibid.*, p. 37. 10. L. J. Thomas, *ibid.*, p. 40. 11. R. C. V. Robinson, *ibid.*, p. 43. 12. S. C. Kaim and I. N. Rosenstein, *ibid.*, p. 46. 13. H. E. Ticktin and J. D. Schultz, *ibid.*, p. 49. 14. J. N. Sussex, *ibid.*, p. 53. 15. I. N. Rosenstein, *ibid.*, p. 57. 16. D. C. English, *Curr. Therap. Res.*, 2:88, 1960. 17. T. H. Harris, *J.A.M.A.*, *172*:1162, 1960. 18. G. L. Usdin, *J. Louisiana M. Soc.*, *112*:142, 1960. 19. I. N. Rosenstein and C. W. Silverblatt, paper read at Pan American Medical Association, 35th Anniversary Congress, Mexico City, Mexico, May 2-11, 1960. 20. K. Rickels, *ibid.* 21. N. Toll, *Dis. Nerv. System*, *21*:264, 1960.

LIBRIUM® Hydrochloride—7-chloro-2-methylamino-5-phenyl-3H-1,4-benzodiazepine 4-oxide hydrochloride

ROCHE LABORATORIES • Division of Hoffmann-La Roche Inc.

Continued from page 939

Dr. Wallis S. Ivy, Duncan, has been presented a Fifty Year Pin by the Oklahoma State Medical Association and a citation for outstanding accomplishment by the Duncan Chamber of Commerce.

The following Oklahoma physicians have been certified by the American Board of Obstetrics and Gynecology: Dr. Paul A. Bischoff, Tulsa; Major Charles R. Cochrane, MC, Fort Sill; Dr. Joseph W. Funnell, Oklahoma City; and Dr. Billie G. Henley, Lawton.

Dr. Stewart G. Wolf, Jr., Oklahoma City, is President-Elect of the American Psychosomatic Society.

SOUTH CAROLINA

Dr. Furman Wallace, Spartanburg, is President of the Tri-State Medical Association.

Four Columbia physicians are among new members of the City of Columbia Board of Health: Drs. L. Palmer Chappelle, E. C. Stevenson, Martin D. Young, and Lee Sanders.

Officers of the South Carolina Trudeau Society are Dr. James W. Fouche, Columbia, President; Dr. Martin M. Teague, Laurens, Vice-President; and Dr. Edmund R. Taylor, Columbia, Secretary-Treasurer.

Dr. Ben N. Miller, Jr., Columbia, has been chosen to represent South Carolina on the governing body of the American Society of Internal Medicine.

Recently certified by the American Board of Obstetrics and Gynecology are Dr. Clarence M. Easley, Greenville; Dr. Samuel P. Fleming, Spartanburg; Dr. Sam M. King, Greenville; and Dr. Robert L. Lumpkin, Georgetown.

TENNESSEE

Officers of the Tennessee State Medical Association are Dr. Ralph O. Rychener, Memphis, President; Dr. William O. Vaughan, Nashville, President-Elect; Drs. William I. Proffitt, Cleveland, J. Kelley Avery, Union City, and C. B. Roberts, Sparta, Vice-Presidents; Dr. Joseph W. Johnson, Jr., Chattanooga, Speaker of the House of Delegates; and Dr. R. H. Kampmeier, Nashville, Secretary-Editor, also Editor of the *Southern Medical Journal*.

The Tennessee Valley Medical Assembly will meet September 26 and 27, 1960 at the Read House in Chattanooga. Dr. Robert A. Waters, 109 Medical Arts Building, Chattanooga, is Chairman.

Dr. Lynn F. Curtis, Maryville, has been appointed Chairman of the Health and Safety Committee of the Blount County Chamber of Commerce.

Dr. Thomas K. Ballard, Jackson, has been named Division Surgeon for the Illinois Central Railroad.

Dr. Morris F. Ferguson, Lebanon, has joined the staff of McFarland Hospital in Lebanon.

Dr. McCarthy DeMere, Memphis, is President of the Sertoma Club.

Dr. Ben Hall, Johnson City, has been inducted as a Fellow of the American College of Physicians.

Continued on page 66

WHAT THIS NEW LOW DOSAGE ANTIHISTAMINE DOES FOR YOUR PATIE

TABLETS Twiston*

Twiston, 2 mg./Twiston R-A, 4 mg.... "Tailor-made" to keep you
(REPEAT ACTION TABLET)
patient symptom-free, alert; without drowsiness or toxici

McNEIL

McNEIL LABORATORIES, INC. • PHILADELPHIA 32, PA.

*Trademark Pat. Pend.

Diagnostic Quandaries

Colitis? Gall Bladder Disease?
Chronic Appendicitis?
Rheumatoid Arthritis? Regional Enteritis?

A DISEASE that is frequently overlooked in solving diagnostic quandaries is amebiasis. Its symptoms are varied and contradictory, and diagnosis is extremely difficult. In one study, 56% of the cases would have been overlooked if the routine three stool specimens had been relied on.[1]

Another study found 96% of a group of 150 patients with rheumatoid arthritis were infected by *E. histolytica*. In 15 of these subjects, nine stool specimens were required to establish the diagnosis.[2]

Webster discovered amebic infection in 147 cases with prior diagnoses of spastic colon, psychoneurosis, gall bladder disease, nervous indigestion, chronic appendicitis, and other diseases. Duration of symptoms varied from one week to over 30 years. In some cases, it took as many as six stool specimens to establish the diagnosis of amebiasis.[3]

Now treatment with Glarubin provides a means of differential diagnosis in suspected cases of amebiasis. Glarubin, a crystalline glycoside obtained from the fruit of *Simarouba glauca*, is a safe, effective amebicide. It contains no arsenic, bismuth, or iodine. Its virtual freedom from toxicity makes it practical to treat suspected cases without undertaking difficult, and frequently undependable, stool analyses. Marked improvement following administration of Glarubin indicates pathologically significant amebic infection.

Glarubin is administered orally in tablet form and does not require strict medical supervision or hospitalization. Extensive clinical trials prove it highly effective in intestinal amebiasis.

Glarubin*

TABLETS

specific for intestinal amebiasis

Supplied in bottles of 40 tablets, each tablet containing 50 mg. of glaucarubin.

Write for descriptive literature, bibliography, and dosage schedules.

1. Cook, J.E., Briggs, G.W., and Hindley, F.W.: Chronic Amebiasis and the Need for a Diagnostic Profile, Am. Pract. and Dig. of Treat. *6*:1821 (Dec., 1955).

2. Rinehart, R.E., and Marcus, H.: Incidence of Amebiasis in Healthy Individuals, Clinic Patients and Those with Rheumatoid Arthritis, Northwest Med., *54*:708 (July, 1955).

3. Webster, B.H.: Amebiasis, a Disease of Multiple Manifestations, Am. Pract. and Dig. of Treat. *9*:897 (June, 1958).

*U.S. Pat. No. 2,864,745

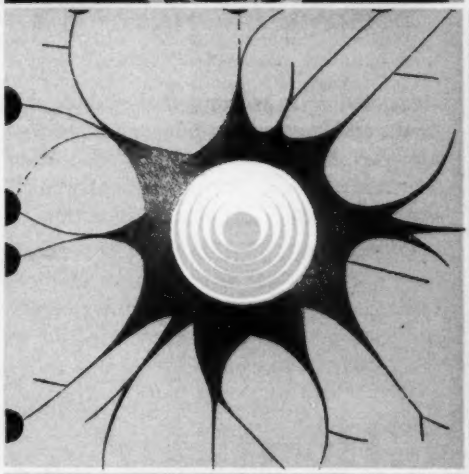
THE S.E. MASSENGILL COMPANY

BRISTOL, TENNESSEE

NEW YORK • KANSAS CITY • SAN FRANCISCO

whenever depression complicates the picture

Tofrānil®
brand of imipramine HCl



hastens recovery

Geigy

In many seemingly mild physical disorders an element of depression plays an insidious etiologic or complicating role.

Because of its efficacy as an antidepressant, coupled with its simplicity of usage, Tofrānil is admirably adapted to use in the home or office in these milder "depression-complicated" cases.

It is always wise to recognize that depression may be an underlying factor . . . that Tofrānil may speed recovery in "hypochondriasis"; in convalescence when recovery is inexplicably prolonged; in chronic illness with dejection; in the menopausal patient whose emotional disturbances resist hormone therapy; and in many other comparable situations in which latent depression may play a part.

Detailed Literature Available on Request

Tofrānil®, brand of imipramine hydrochloride, tablets of 25 mg. Ampuls for intramuscular administration, 25 mg. in 2 cc. of solution.

Geigy, Ardsley, New York

160-60

The physician listens to a tense, nervous patient discuss her emotional problems. To help her, he prescribes Meprospan (400 mg.), the only continuous-release form of meprobamate.

The patient takes one Meprospan-400 capsule at breakfast. She has been suffering from recurring states of anxiety which have no organic etiology.

She stays calm while on Meprospan, even under the pressure of busy, crowded supermarket shopping. And she is not likely to experience any autonomic side reactions, sleepiness or other discomfort.

She takes another capsule of Meprospan-400 with her evening meal. She has enjoyed sustained tranquilization all day—and has had no between-dose letdowns. Now she can enjoy sustained tranquilization all through the night.

Relaxed, alert, attentive . . . she is able to listen carefully to P.T.A. proposals. For Meprospan does not affect either her mental or her physical efficiency.

Peacefully asleep . . . she rests, undisturbed by nervousness or tension. (Meprospan literature is available from Wallace Laboratories, Cranbury, N. J.)

anorectic-ataractic

BAMADEX®

meprobamate 400 mg., with d-amphetamine sulfate 5 mg., Tablets

FOR THERAPY
OF OVERWEIGHT PATIENTS

- d-amphetamine depresses appetite and elevates mood
- meprobamate eases tensions of dieting (yet without overstimulation, insomnia or barbiturate hangover).

Dosage: One tablet one-half to one hour before each meal.

A LOGICAL COMBINATION
IN
APPETITE CONTROL

Lederle

The Janis Clinic

—for the treatment of ***obesity***

Green Springs, Ohio

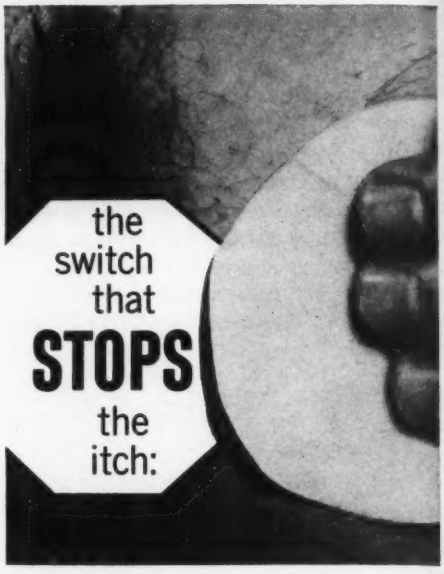
A clinic for the treatment of obese adults and children:

- DIET MANAGEMENT
- EXERCISE
- MEDICATION
- PSYCHOTHERAPY

Facilities for obese female and male children, ages 10-18, available only during the months of July and August.

For more detailed information, write or phone:

THE JANIS CLINIC, Green Springs, Ohio
Phone 4151
Leo B. Janis, M.D., *Medical Director*



FROM *harsh, irritant toilet paper*

TO *gentle, soothing*

TUCKS®

–soft, cotton flannel pads saturated with witch hazel (50%) and glycerin (10%), pH 4.6

Routine use of moist, antipruritic TUCKS after defecation improves many intractable cases of pruritus ani and is a valuable adjunct to specific therapy. In milder cases, regular cleansing with TUCKS is often curative.

Try TUCKS . . . for your next pruritus patient. Jars of 40 and 100.

Please send me a sample supply of TUCKS.

_____ **M. D.**

Address _____

City _____ **Zone** ____ **State** _____

fuller

FULLER PHARMACEUTICAL COMPANY
3108 W. Lake Street
Minneapolis 16, Minnesota

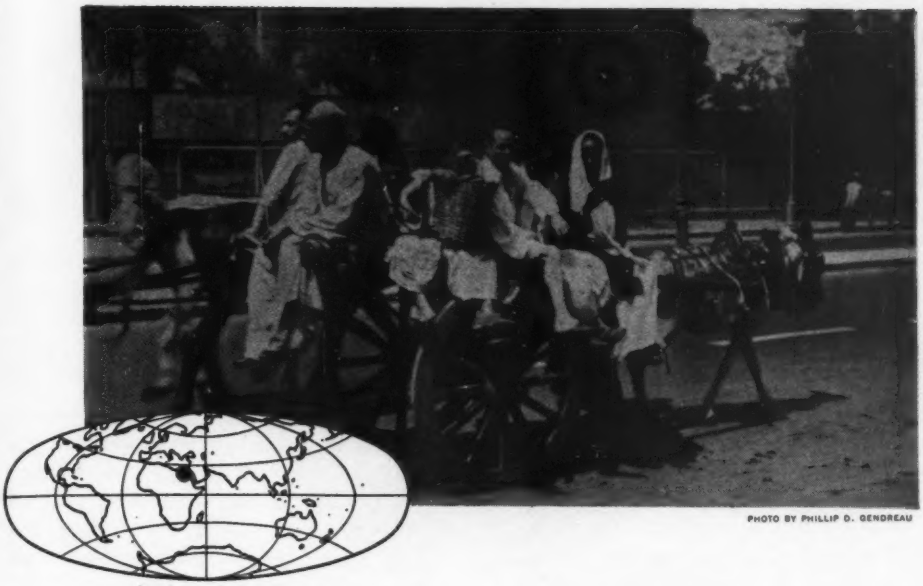


PHOTO BY PHILLIP D. GENDREAU

world-wide evidence favors Furoxone for bacterial diarrheas

In Egypt, Furoxone® effective against shigella strains now resistant to other antimicrobials

Cairo investigators administered FUROXONE for one week to 37 patients with shigellosis, reported all 37 clinically cured, 35 free of shigella prior to completion of FUROXONE therapy.

FUROXONE was tested in light of evidence that shigella strains resistant to sulfonamides, tetracyclines and chloramphenicol now exist. Observations: "All shigella isolated were sensitive in vitro to [FUROXONE]". Clinically, FUROXONE "significantly reduces the duration and severity of the diarrhea and effects bacteriological cure .... The absence of toxic or side effects gives [FUROXONE] an advantage not possessed by the other drugs in current use."

Musgrave, M. E. and Arm, H. G.: Antibiotic Med. & Clin. Therapy 7:17 (Jan.) 1960.

FUROXONE LIQUID: a pleasant orange-mint flavored suspension containing FUROXONE 50 mg. per 15 cc., with kaolin and pectin ■ for patients of all ages (may be mixed with infant formulas, passes through a standard nursing nipple) ■ Supply: bottles of 240 cc. **FUROXONE TABLETS:** 100 mg., scored, bottles of 20 and 100.

DOSAGE: should provide (in 4 divided doses) 400 mg. daily for adults, 5 mg./Kg. daily for children.

FUROXONE

THE NITROFURANS —a *unique* class of antimicrobials
EATON LABORATORIES, NORWICH, NEW YORK

AN AMES CLINIQUICK®
CLINICAL BRIEFS FOR MODERN PRACTICE

WHAT LABORATORY PROCEDURES ARE INDICATED IN DIABETICS WITH URINARY TRACT INFECTIONS?

A urine culture is absolutely essential in the diabetic suspected of having a urinary tract infection since such infection is not always accompanied by pyuria. It is also essential to keep the urine free from sugar—as shown by frequent urine-sugar tests—for successful therapy.

Source: Harrison, T. R., *et al.:* Principles of Internal Medicine, ed. 3, New York, McGraw-Hill Book Co., 1958, p. 620.

the most effective method of routine testing for glycosuria...
color-calibrated

CLINITEST®
BRAND *Reagent Tablets*

the *standardized* urine-sugar test for reliable quantitative estimations

Urinary tract infections are about four times more frequent in the diabetic than in the non-diabetic. The prevention and treatment of urinary tract infections, as well as the avoidance of other complications of diabetes, are significantly more effective in the well-controlled diabetic. The patient should be impressed repeatedly with the importance of continued daily urine-sugar testing—especially during intercurrent illness—and warned of the consequences of relaxed vigilance.

"urine-sugar profile" With the new *Graphic Analysis Record* included in the CLINITEST Urine-Sugar Analysis Set (and in the tablet refills), daily urine-sugar readings may be recorded to form a graphic portrayal of glucose excretion most useful in clinical control.

- *motivates patient cooperation* through everyday use of Analysis Record
- *reveals at a glance day-to-day trends* and degree of control
- *provides a standardized color scale* with a complete range in the familiar blue-to-orange spectrum

84460

AMES
COMPANY, INC
Elkhart • Indiana
Toronto • Canada

guard against ketoacidosis ... test for ketonuria for patient and physician use

ADDED SAFETY FOR DIABETIC CHILDREN
ACETEST® *Reagent Tablets*
KETOSTIX® *Reagent Strips*

For demonstrably greater relief in asthma[1]

BRONKOTABS®

CLEARS the bronchial tree of thick mucus and DILATES the bronchioles

Bronkotabs is more effective because it is more comprehensive in treatment. First, Bronkotabs dilates bronchioles, combats local edema and provides mild sedation.

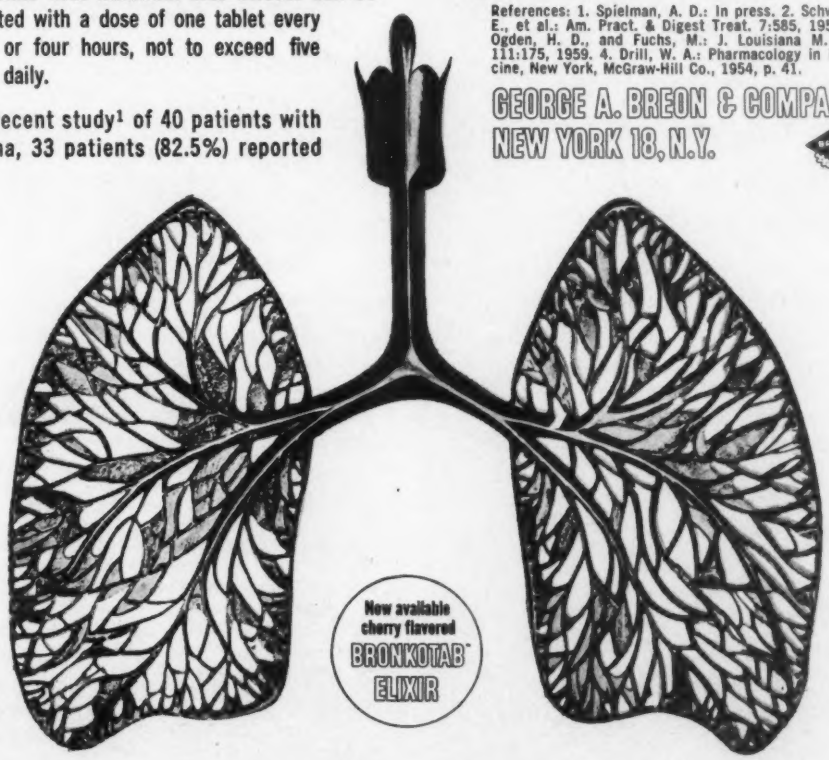
In addition, Bronkotabs decongests, using a most effective expectorant (glyceryl guaiacolate)[2] to liquefy and help expel the thick, tenacious mucus which is the cause of much of the respiratory distress in chronic asthma.[3] Since asthma is a chronic allergic disease of the bronchial tree,[3] Bronkotabs also supplies a highly efficient antihistamine (thenyldiamine) for prophylactic maintenance.[4] Marked and consistent relief of symptoms with minimum side effects can be expected with a dose of one tablet every three or four hours, not to exceed five times daily.

In a recent study[1] of 40 patients with asthma, 33 patients (82.5%) reported Bronkotabs brought fair to good relief from asthmatic symptoms. Asthma relief was expressed by ease of expectoration of secretions, reduction of bronchospasm, and increased vital capacity. "The combination of drugs used in . . . [BRONKOTABS] . . . gave greater relief in these patients than the conventionally used tablet [ephedrine, theophylline, phenobarbital] . . ."

BRONKOTABS DOES MORE FOR THE ASTHMATIC BECAUSE IT IS MORE COMPREHENSIVE IN ACTION. Each tablet contains: Theophylline 100 mg.; Ephedrine Sulfate 24 mg.; Phenobarbital 8 mg.; Thenyldiamine HCl 10 mg. and Glyceryl Guaiacolate 100 mg.
Supplied: bottles of 100 white scored tablets.

References: 1. Spielman, A. D.: In press. 2. Schwartz, E., et al.: Am. Pract. & Digest Treat. 7:585, 1956. 3. Ogden, H. D., and Fuchs, M.: J. Louisiana M. Soc. 111:175, 1959. 4. Drill, W. A.: Pharmacology in Medicine, New York, McGraw-Hill Co., 1954, p. 41.

GEORGE A. BREON & COMPANY
NEW YORK 18, N.Y.



Digitalis

in its completeness

Each pill is equivalent to one USP Digitalis Unit

Physiologically Standardized therefore always dependable.

Clinical samples sent to physicians upon request.

Davies, Rose & Co., Ltd.
Boston, 18, Mass.

BAMADEX

meprobamate 400 mg., with d-amphetamine sulfate 5 mg., tablets

anorectic-ataractic

A logical combination for appetite suppression

meprobamate **plus** d-amphetamine...suppresses appetite...elevates mood... reduces tension...**without** insomnia, overstimulation or barbiturate hangover.

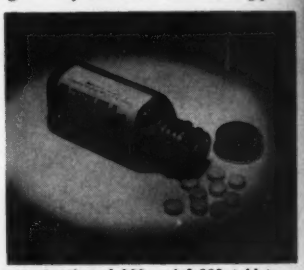
Dosage: One tablet one-half to one hour before each meal.

Lederle

VADRIN Antihistaminic Tablets

for Allergies of Diverse Etiology

ALLERGIES due to Colds, Foods, Drugs, Dust and Pollens



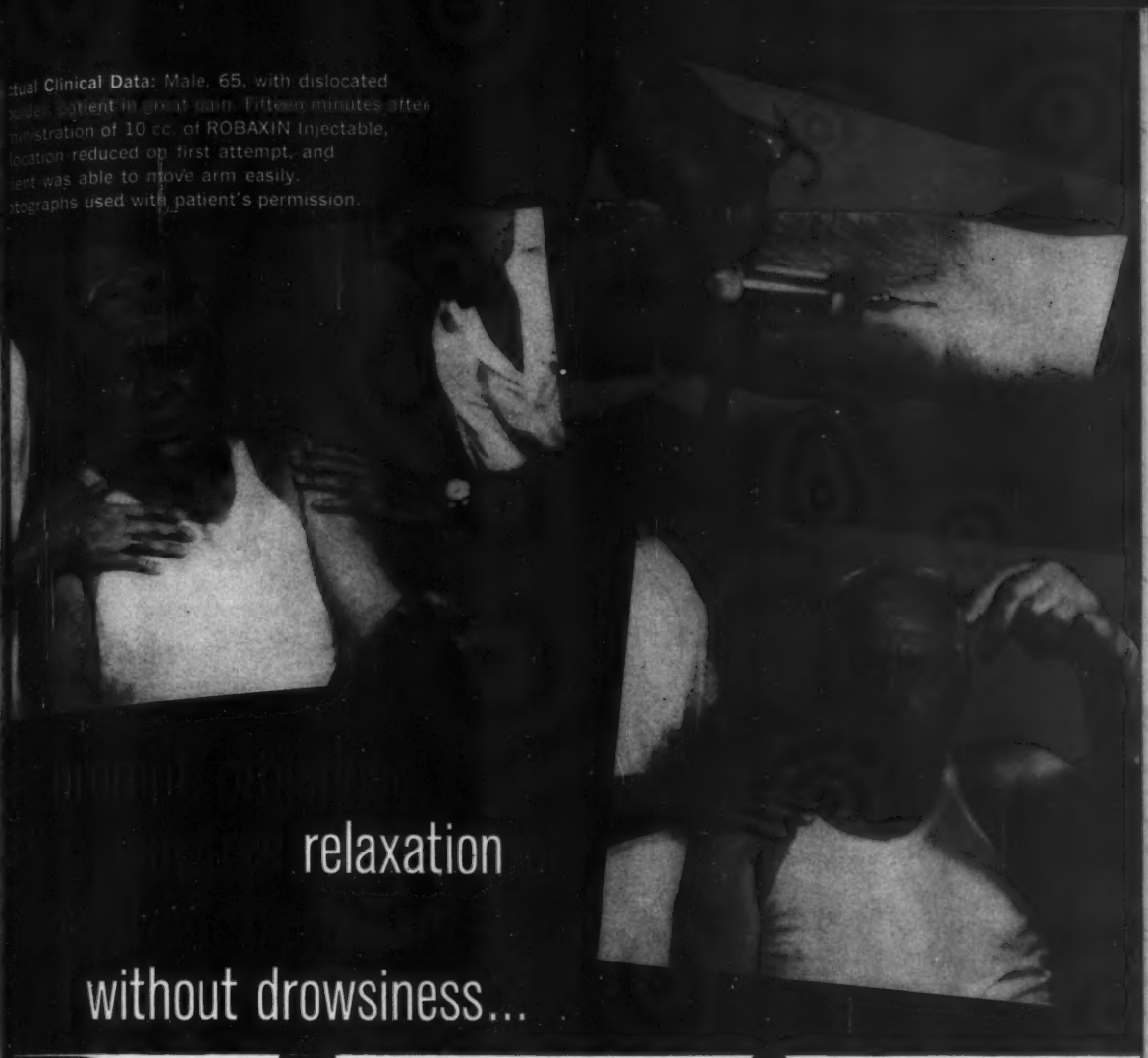
In bottles of 100 and 1,000 tablets

VADRIN tablets provide a dual antihistaminic action for faster and more effective relief of allergies due to colds, foods, drugs, dust and pollens. They combine two standard antihistaminics: namely, chlorpheniramine maleate and methapyrilene hydrochloride.

VADRIN FORTIS tablets contain the same ingredients in double the amount.

HISTA-VADRIN tablets contain an additional antihistaminic ingredient: namely, phenylpropanolamine hydrochloride.

FIRST TEXAS *Pharmaceuticals, Inc.*
Pharmaceuticals Since 1901
DALLAS ATLANTA


tual Clinical Data: Male, 65, with dislocated
patient in great pain. Fifteen minutes after
inistration of 10 cc. of ROBAXIN Injectable,
location reduced on first attempt, and
ent was able to move arm easily.
tographs used with patient's permission.

relaxation

without drowsiness...

Robaxin®

Robins

carbamol 'Robins' U.S. Pat. No. 2770649

ROBAXIN Injectable: for relaxation of painful spasm within minutes.

ROBAXIN Tablets: for initial relief, or to maintain relaxation originally induced by ROBAXIN Injectable. Virtually free from adverse side effects, including drowsiness.

Ten published studies show ROBAXIN Injectable and ROBAXIN Tablets beneficial in 91% of cases.[1-10] Literature available to physicians on request.

SUPPLY: ROBAXIN Tablets, 0.5 Gm. (white, scored) in bottles of 50 and 500.

ROBAXIN Injectable, each ampul containing 1.0 Gm. of methocarbamol in 10 cc. of sterile solution.

A. H. ROBINS CO., INC., Richmond 20, Virginia

CLASSIFIED ADVERTISEMENTS

WANTED—Internist to establish own practice in a south Georgia city. Write CRW, c/o SMJ giving full credentials in first letter.

WANTED—Two Internists. Board certification or eligibility desirable but not essential. U. S. citizenship and licensure required. Some quarters available; physical plant one of finest in Nation. Contact: Manager, VA Center, Dublin, Georgia.

FOR SALE—Complete equipment for doctors office handling full medical and surgical practice; examining and treatment rooms, small laboratory, files, etc. Patients' records available for doctor buying practice and equipment or equipment can be bought separately. Located in the heart of Albany. Contact: Mrs. H. M. McKemie, 1201 North Davis Street, Albany, Georgia.

FOR SALE OR PURCHASE—Used medical and x-ray equipment. A. H. Smullian & Company, P. O. Box 6112 Station H, Atlanta, Georgia.

FOR SALE, RENT OR LEASE—Attractive, well-located clinic with going General Practice. Available July 1, 1960. Contact: M. B. Harthcock, M.D., Clarksdale, Mississippi.

INTERNIST WANTED—Small southern Virginia town; nearby teaching and recreational facilities; expanding clinic and hospital (privately owned). Open salary two years; then partnership with excellent financial future. Needed now but will wait for proper man. Contact: WRW, c/o SMJ.

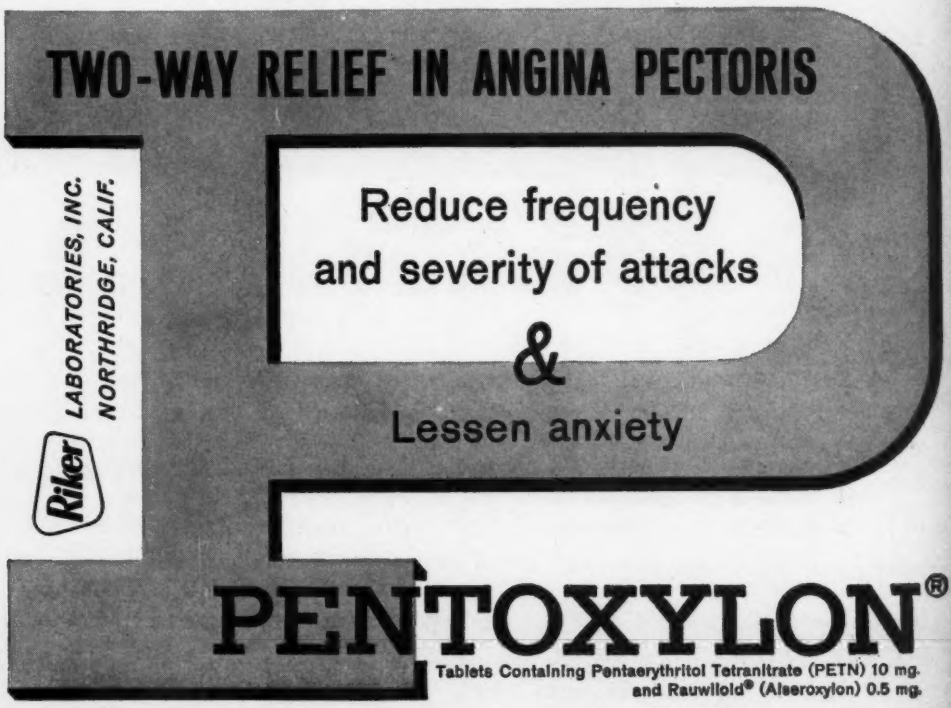
PRACTICE FOR SALE—General practice in town of 7,800. Completely equipped office, x-ray, air conditioned, near 96-bed hospital. $6,000 for equipment, $2,000 cash, balance reasonable terms. Retiring due to health. Contact: John C. Hart, M.D., Paris, Kentucky, or Parker Bradley, Executive Vice President, First National Bank, Paris, Kentucky.

FOR SALE—Keleket radiographic-fluoroscopic x-ray machine with tube stand and accessories. Capacity 30 MA at 90 kilovolts shock proof. Used very little in obstetrical practice. Very low price. Call Atlanta TR 4-0477 or contact HC, c/o SMJ.

AVAILABLE—Radiologist for "Locum Tennens." Contact: Dr. A. W. Brown, 404 Woodside Drive, Shelby, North Carolina.

WANTED—Pathologist to direct Department of Pathology. 180-bed hospital; fully accredited; intern training; opportunity for advancement; modern department; excellent income; contract open. Apply: Robert M. Murphy, Administrator, Floyd Hospital, Rome, Georgia.

WANTED—Position in career civil service for beginning or experienced Physical Therapist in Physical Medicine & Rehabilitation Service of 950-bed hospital-domiciliary center. Starting salary $4,980 per annum. $150 annual increments, excellent leave, retirement, insurance benefits. Write or call Personnel Officer, Veterans Administration Center, Dublin, Georgia.


TWO-WAY RELIEF IN ANGINA PECTORIS
Reduce frequency and severity of attacks
&
Lessen anxiety
Riker LABORATORIES, INC. NORTHRIDGE, CALIF.
PENTOXYLON®
Tablets Containing Pentaerythritol Tetranitrate (PETN) 10 mg. and Rauwiloid® (Alseroxylon) 0.5 mg.

suturing: Xylocaine® HCl Solution applied topically will permit cleaning and suturing of wounds with patient comfort in an emergency or in the office. Fast acting – Safe – Dependable.

bursitis: Xylocaine HCl Solution injected into the painful area will diffuse around the bursae relieving pain promptly – often restoring normal freedom of motion. Prolonged anesthesia often prevents recurring pain.

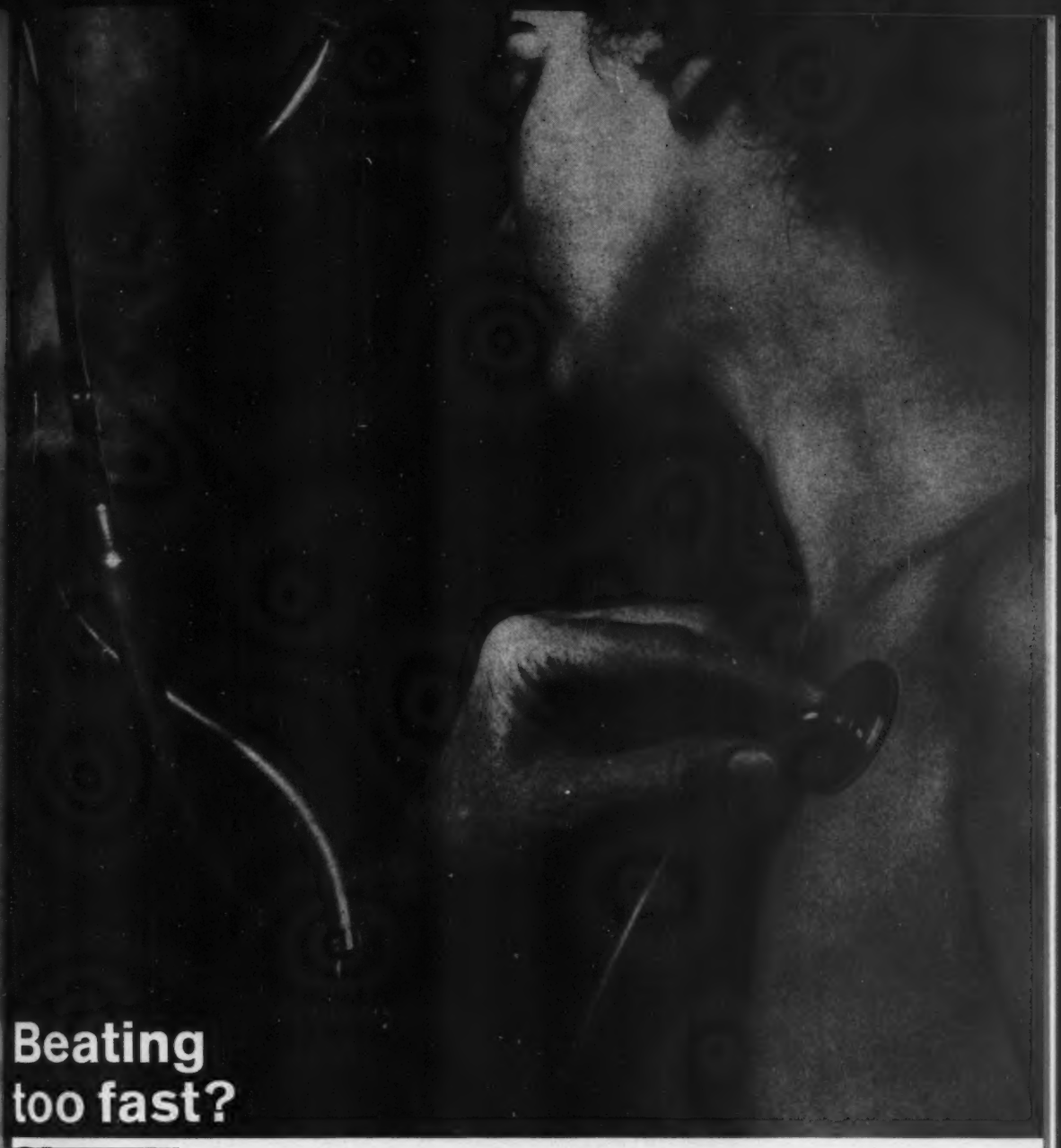
therapeutic block: Xylocaine HCl Solution interrupts the underlying mechanism of pain, with relief often persisting even after the block has disappeared. It is of value in assisting motion or manipulation; for severe, intractable pain conditions; and in allowing patient comfort for other procedures.

minor surgery: Xylocaine HCl Solution will diffuse over a wide operative field, permitting pain-free removal of warts, cysts, moles, etc., and giving safe, effective, and predictable anesthesia for patient comfort.

Supplied: Multiple dose vials, 20 cc. and 50 cc.; 0.5%, 1% and 2% without and with epinephrine 1:100,000. Ampules, 2 cc.; 2% without and with epinephrine 1:100,000.

ASTRA

*U.S. PAT. NO. 2,441,498 MADE IN U.S.A.



Beating too fast?

Slow it down with SERPASIL®

(reserpine CIBA)

Serpasil has proved effective as a heart-slowing agent in the following conditions: mitral disease; myocardial infarction; cardiac arrhythmias; neurocirculatory asthenia; thyroid toxicosis; excitement and effort syndromes; cardiac neurosis; congestive failure. Serpasil should be used with caution in patients receiving digitalis and quinidine. It is not indicated in cases of aortic insufficiency.

SUPPLIED: Tablets, 0.1 mg., 0.25 mg. (scored) and 1 mg. (scored). Complete information available on request.

CIBA

SUMMIT • NEW JERSEY

TO PROMOTE

Resistance to Stress

THROUGH

Total Care OF THE PATIENT

Susceptibility to the effects of stress, physical or psychic, is aggravated by a poor nutritional state; **resistance and recovery are promoted by enhanced nutrition.**

In repair, use of energy and amino acids is increased with concomitant increase in demand for vitamins of the B complex. In many clinics, VITA-FOOD Brewers' Yeast is a routine, a vital aid to **total care** of the patient—emphasized anew as the rationally inclusive approach to ideal treatment.

VITA-FOOD Brewers' Yeast

Continued from page 54

Dr. Earle L. Wrenn, Jr., Memphis, is President of the Memphis Better Schools Committee.

Dr. E. Wayne Gilley, Chattanooga, and Dr. I. F. Tullis, Memphis, have been chosen to represent Tennessee on the Governing Body of the American Society of Internal Medicine.

Dr. Lindsay K. Bishop is President and Dr. Lowry D. Kirby, Secretary-Treasurer, of the Nashville Pediatric Society.

Tennessee physicians who have been certified by the American Board of Obstetrics and Gynecology recently include Dr. Floyd N. Bankston, Knoxville; Dr. Robert W. Boatwright, Chattanooga; Dr. John C. Burch, Nashville; Dr. Sidney D. Jones, Jr., Memphis; and Dr. Margaret E. Joyce, Knoxville.

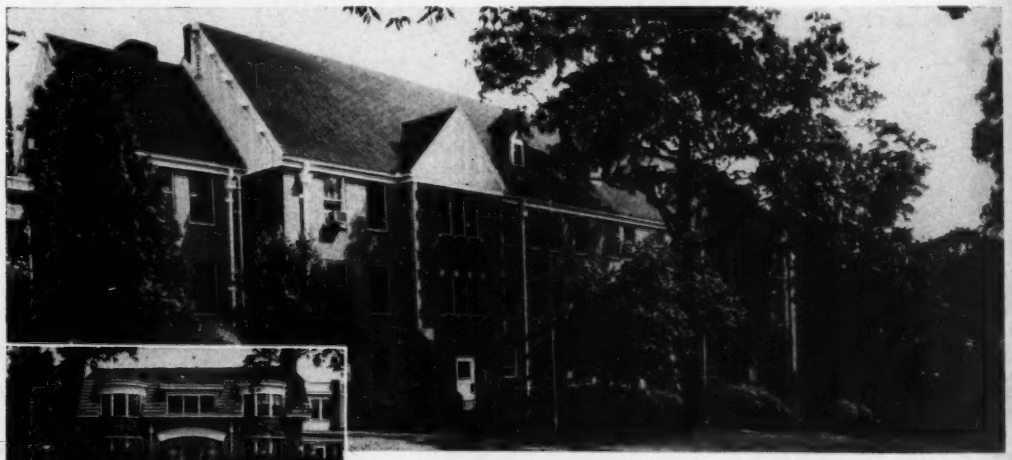
The Tennessee Radiological Society has elected the following officers: Dr. George K. Henshall, Jr., Chattanooga, President; Dr. Ed H. Mabry, Memphis, President-Elect; Dr. M. D. Ingram, Jr., Nashville, Vice-President; and Dr. James J. Range, Johnson City, Secretary-Treasurer.

Dr. Sam H. Sanders, Memphis, is President of the American Society of Facial Plastic Surgery.

TEXAS

Dr. Milford O. Rouse, Dallas, Past President of the Southern Medical Association and a member of its

Continued on page 68



Out-Patient Clinic and Offices

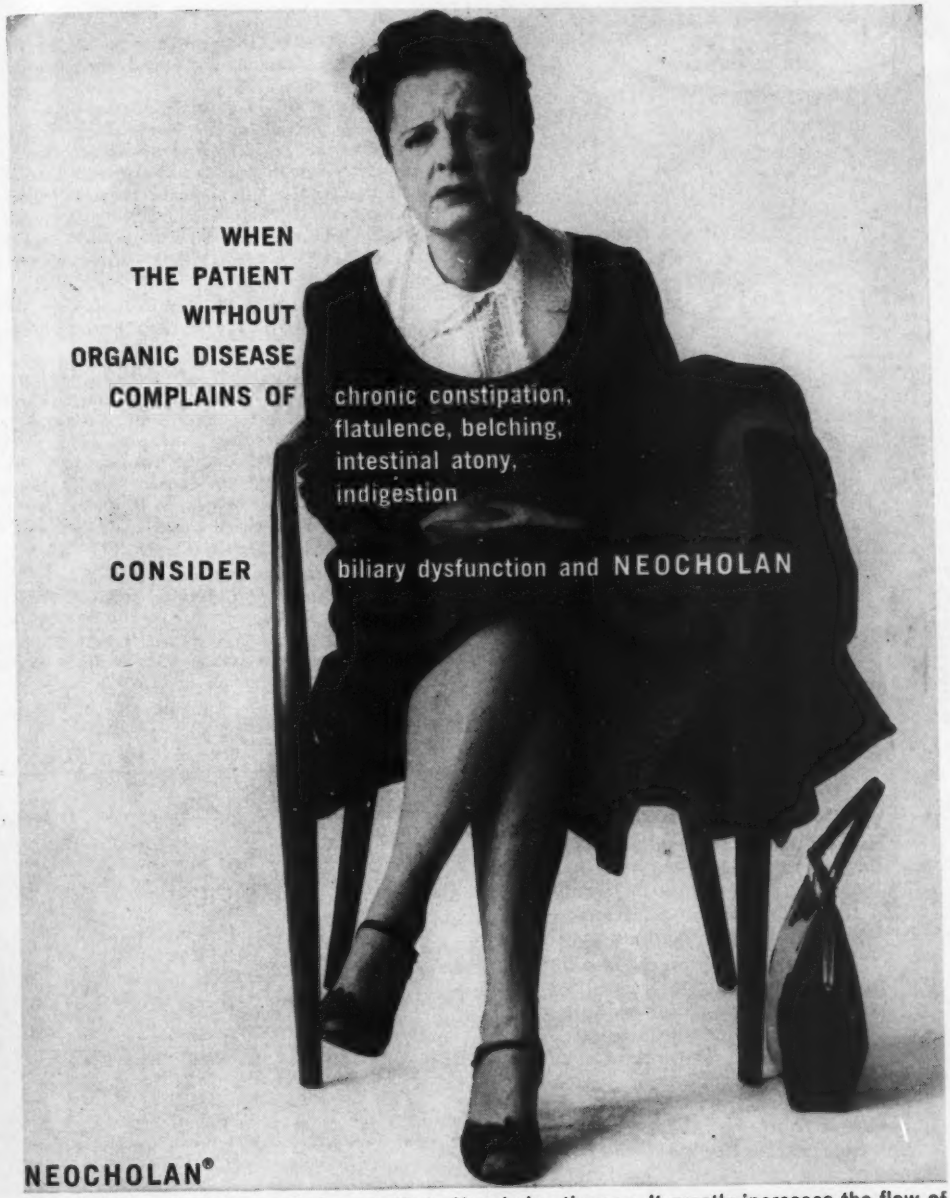
HILL CREST SANITARIUM

Established in 1925

FOR NERVOUS AND MENTAL DISEASES AND ADDICTION PROBLEMS

James A. Becton, M.D. James Keen Ward, M.D.

P. O. Box 2896, Woodlawn Station, Birmingham 6, Ala. Phone WO 1-1151 and WO 1-1152

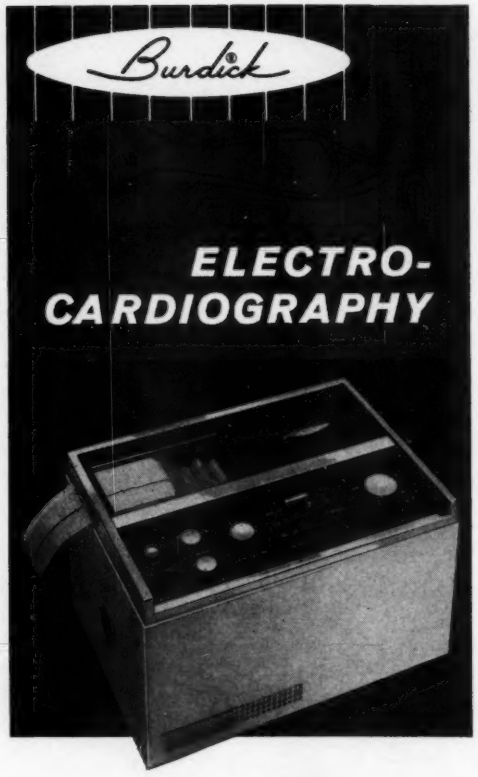


NEOCHOLAN®

Your patient will often respond promptly to Neocholan therapy. It greatly increases the flow of thin, nonviscid bile and corrects biliary stasis by flushing the biliary system. It also relaxes intestinal spasm, resulting in an unimpeded flow of bile and pancreatic juice into the small intestine. Neocholan helps to promote proper digestion and absorption of nutrients. It also encourages normal peristalsis by restoring intestinal tone.

Each tablet provides: Dehydrocholic Acid Compound, P-M Co. 265 mg. (Dehydrocholic Acid, 250 mg.); Homatropine methylbromide 1.2 mg.; Phenobarbital 8.0 mg. Supplied in bottles of 100 tablets.

PITMAN-MOORE COMPANY
DIVISION OF ALLIED LABORATORIES, INC.
INDIANAPOLIS, INDIANA



. . . an integral part of modern practice

Has the diagnostic equipment in your office kept pace with your own knowledge of new drugs, medicines and therapeutic technics? If not—call in your Burdick man!

He'll bring you up to date on the latest advances in electromedical instrumentation—as for example, the Burdick dual-speed electrocardiograph. Determine your net cost of new equipment, taking into consideration the income tax savings from annual depreciation allowances. This can make the purchase of new professional equipment far more attractive financially than you may have realized!

THE BURDICK CORPORATION
Milton, Wisconsin
Branch Offices: New York • Chicago • Atlanta • Los Angeles
Dealers in all principal cities

Burdick

Continued from page 66

Board of Trustees, addressed the Society of Professional Business Consultants during their sessions in Chattanooga on May 16.

Miss Harriet Cunningham, Managing Editor of the *Texas State Journal of Medicine*, and a member of the staff of the Texas Medical Association since 1945, passed away May 8. Friends and associates have established the Harriet Cunningham Memorial Graduate Fellowship in Medical Writing at the University of Texas. Contributions may be made to the Texas Medical Association, and specifically earmarked for the Fellowship fund.

Dr. G. V. Brindley, Jr., Temple, has been elected Secretary-Treasurer of the Southern Society of Clinical Surgeons.

Several Texas physicians have recently been certified by the American Board of Obstetrics and Gynecology: Dr. Robert H. Benbow, Bryan; Dr. Donald P. Bernard, Corpus Christi; Dr. Andy J. Bowden, Jr., Fort Worth; Dr. Robert V. Colpitts, Houston; Dr. Joe D. Crawford, Jacksonville; Dr. Harold I. Daily, Houston; Major Charles F. Ford, Lubbock; Dr. James H. Goodson, Dallas; Dr. Michael Kurilecz, Dallas; and Dr. Donald E. McGuire, Dallas.

Officers of the International Medical Assembly of Southwest Texas are Dr. Max E. Johnson, President; Dr. Lawrence B. Reppert, President-Elect; Dr. A. P. Thaddeus, First Vice-President; Dr. John M. Smith, Jr., Second Vice-President; and Dr. William M. Center, Secretary-Treasurer, all of San Antonio.

Dr. Pat I. Nixon, San Antonio, and Dr. Willard R.

Continued on page 70

A logical prescription for overweight patients

anorectic-ataractic

BAMADEX®

meprobamate 400 mg., with d-amphetamine sulfate 5 mg., Tablets

meprobamate **plus** d-amphetamine... depresses appetite...elevates mood... eases tensions of dieting...**without** overstimulation, insomnia or barbiturate hangover.

Dosage: One tablet one-half to one hour before each meal.

Lederle

For the irritable G.I. tract

Milpath acts quickly to suppress hypermotility, hypersecretion, pain and spasm, and to allay anxiety and tension with minimal side effects.

AVAILABLE IN TWO POTENCIES

MILPATH-400—Yellow, scored tablets of 400 mg. Miltown (meprobamate) and 25 mg. tridihexethyl chloride.
Bottle of 50.
Dosage: 1 tablet t.i.d. at mealtime and 2 at bedtime.

MILPATH-200—Yellow, coated tablets of 200 mg. Miltown (meprobamate) and 25 mg. tridihexethyl chloride.
Bottle of 50.
Dosage: 1 or 2 tablets t.i.d. at mealtime and 2 at bedtime.

Milpath®

®Miltown + *anticholinergic*

WALLACE LABORATORIES *New Brunswick, N. J.*

Continued from page 68

Cooke, Galveston, have been elected to emeritus membership in the Texas Medical Association, one of the highest honors it can bestow.

General Practitioner of the Year in Texas is Dr. Elbert Dean Rice, Tyler.

Officers of the Top o' Texas Medical Society are Dr. Richard D. Falkenstein, Pampa, President; Dr. Woodrow W. Massad, Borger, President-Elect and Vice-President; and Dr. T. DeWitt Harvey, Pampa, Secretary-Treasurer.

The Victoria-Calhoun-Goliad Medical Society announces the following officers: Dr. Richard C. Allen, Jr., Victoria, President; Dr. F. M. Logsdon, Port Lavaca, Vice-President; and Dr. Ben H. White, Victoria, Secretary-Treasurer.

Treasurer of the American Radium Society is Dr. Gilbert H. Fletcher, Houston.

Dr. James W. Crawley, Houston, is Treasurer of the American Epilepsy Society.

VIRGINIA

Dr. Hugh Trout, Jr., Roanoke, is President of the Southern Society of Clinical Surgeons.

Newly-elected to fellowship in the New York Academy of Sciences is Dr. Walter H. Hartung, Medical College of Virginia.

Chief of Staff at the John Randolph Hospital in

Continued on page 72

TUCKER HOSPITAL, INC.

212 West Franklin St.

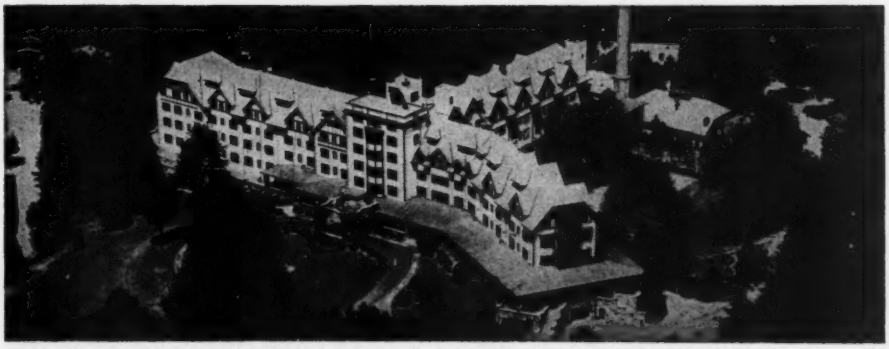
RICHMOND, VIRGINIA

A private hospital for diagnosis and treatment of psychiatric and neurological patients. Hospital and out-patient services.

(Organic diseases of the nervous system, psychoneuroses, psychosomatic disorders, mood disturbances, social adjustment problems, involutional reactions and selective psychotic and alcoholic problems.)

DR. JAMES ASA SHIELD DR. WEIR M. TUCKER
DR. GEORGE S. FULTZ, JR. DR. AMELIA G. WOOD

Appalachian Hall • ESTABLISHED 1916 Asheville, North Carolina



An Institution for the diagnosis and treatment of Psychiatric and Neurological illnesses, rest, convalescence, drug and alcohol habituation.

Insulin Coma, Insulin Sub-Shock, Electroshock and Psychotherapy are employed. The Institution is equipped with complete laboratory facilities including electroencephalography and X-ray.

Appalachian Hall is located in Asheville, North Carolina, a resort town, which justly claims an all around clime for health and comfort. There are ample facilities for classification of patients, rooms single or en suite.

WM. RAY GRIFFIN, JR., M.D. MARK A. GRIFFIN, M.D.
ROBERT A. GRIFFIN, M.D. MARK A. GRIFFIN, JR., M.D.

For rates and further information write APPALACHIAN HALL, ASHEVILLE, N. C.

" . . . Well, I always prescribe Rorer's Maalox. It's an excellent antacid, doesn't constipate and patients will take it indefinitely."

MAALOX® an efficient antacid suspension of magnesium-aluminum hydroxide gel offered in bottles of 12 fluidounces.

TABLET MAALOX: 0.4 Gram (equivalent to one teaspoonful), Bottles of 100.

TABLET MAALOX No. 2: 0.8 Gram, double strength (equivalent to two teaspoonfuls), Bottles of 50 and 250.

Samples on request.

WILLIAM H. RORER, INC., Philadelphia 44, Pennsylvania

Continued from page 70

Hopewell is Dr. J. G. Easterling. Assistant Chief of Staff is Dr. A. T. Brickhouse, and Secretary is Dr. W. P. Youngblood.

Officers of the Hampton Medical Society are Dr. Helen Dorsey, Hampton, President; Dr. Philip Murray, Newport News, Vice-President; and Dr. L. M. Lieberman, Hampton, Secretary-Treasurer.

Dr. John W. Gales, Galax, is Health Director of the Carroll-Grayson-Galax Health District and Dr. Marion Edmonds is Director of the Henry-Patrick-Martinsville Health District.

New members of The Medical Society of Virginia are Dr. George W. Basany, Falls Church; Dr. David M. Brillhart, Abingdon; Dr. Charlotte P. Donlan, Falls Church; Dr. John T. Edmonds, Accomac; Dr. Samuel T. Ellis, Richmond; Dr. Edward H. Hancock, Jr., Lynchburg; Dr. William L. Harris, Falls Church; Dr. Claude K. Hylton, Manassas; Dr. Hubert A. Marshall, Charlottesville; Dr. Harry M. McDermott, Fairfax; Dr. Edward C. Paarfus, Jr., Stuart; Dr. Carlos A. Recio, Staunton; Dr. Victor Skorapa, Jr., Pulaski; Dr. Thomas U. Vermillion, Hampton; Dr. Thomas E. Wheless, Roanoke; and Dr. Ruth F. Williams, Richmond.

The following Virginia physicians have recently been certified by the American Board of Obstetrics and Gynecology: Dr. William M. Bangel, Newport News; Dr. Richard R. Chamberlain, Roanoke; Dr. William A. Cook, Jr., Lynchburg; Dr. Clifford H. Fox, Charlottesville; Dr. Francis S. Gardner, MC, Langley AFB; Dr. Louis H. Keffer, Jr., Warwick; and Dr. Dean H. Martin, Arlington.

WEST VIRGINIA

Officers of the West Virginia Academy of Ophthalmology and Otolaryngology are Dr. John A. B. Holt, Charleston, President; Dr. Albert C. Esposito, Huntington, President-Elect, and Secretary of the Section on Ophthalmology and Otolaryngology for Southern Medical Association; Dr. William K. Marple, Huntington, Vice-President; Dr. Worthy W. McKinney, Beckley, Secretary-Treasurer; and Dr. R. Alan Fawcett, Wheeling, Director.

Dr. Larry C. Smith, Ceredo, is Health Officer for Wayne County.

Dr. Ray E. Burger, Welch, is President of the West Virginia Chapter of the American College of Surgeons; Dr. Victor S. Skaff, Charleston, is Vice-President; and Dr. Jack C. Morgan, Fairmont, is Secretary-Treasurer.

Dr. Bernard Zimmermann has been appointed Professor and Head of the Department of Surgery at the West Virginia University School of Medicine.

Dr. Julius L. Berkley, Charleston, has been certified by the American Board of Proctology.

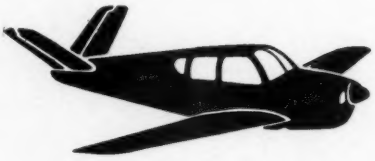
New honorary life members of the West Virginia State Medical Association are Drs. H. Allen Whisler and Eugene B. Wright, Clarksburg; Dr. G. G. Irwin, Charleston; Dr. R. E. Woodall, Coral Gables, Florida; Dr. Henry C. Hays, Williamson; Dr. H. V. King, Morgantown; and Dr. Rush C. Newman, Spencer.

Recently certified by the American Board of Obstetrics and Gynecology were Dr. Robert T. Brandfass, Wheeling, and Dr. Daniel A. Mairs, Charleston.

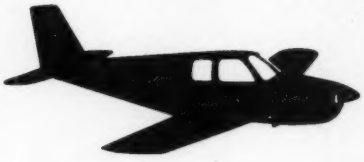
in severe mental and emotional stress, Thorazine®, one of the fundamental drugs brand of chlorpromazine **in medicine, provides prompt control of symptoms—especially agitation and hostility.**

SMITH KLINE & FRENCH

First Choice
OF PROFESSIONAL MEN



BEECHCRAFT BONANZA



BEECHCRAFT DEBONAIR

Choice of Models and Colors in Stock for Delivery

For Descriptive Literature Write or Call

HAL SPRAGINS, III, Atlanta **WILLIAM C. SHILLINGLAW, Charlotte**

Southern Airways Company

ATLANTA AIRPORT
ATLANTA, GEORGIA **TEL. POplar 7-3766**

Charlotte, N. C., Tel. FRanklin 6-7150 *Birmingham, Ala., Tel. FAirfax 2-0502*
Tampa, Fla., Tel. 2-3363 *Orlando, Fla., Tel. CHerry 1-1585*

BIBLIOGRAPHY

1. J. Pharm. & Exp. Ther. 89:131
2. J. Urology 73:487
3. J. Mo. Med. Assoc. 48:685
4. Med. Rec. & Annals 43:1104

IN G. I. OR G. U. SPASM

Thioethylamine (-$SCH_2CH_2N<$), nucleus of the Trocinate molecule, is common to enzymes involved in the contraction of smooth muscle cells. Sulfur, the key atom of the thioethylamine group, is also basic to the chemistry of muscle contractions, entering into the essential reversible oxidation-reduction reactions. These identities suggest that the strong, direct inhibiting action of Trocinate upon muscle-cell contraction, independent of general suppression of the parasympathetic nervous system, is that of a true anti-metabolite. Skeletal muscles are not affected.

Comprehensively evaluated pharmacologically[1] and clinically[2,3,4], Trocinate is a potent and dependable antispasmodic, yet is remarkably free from side-effects, and will not cause mydriasis, anuria, or tachycardia. Its antisialogogue effect is extremely low.

Dosage: **The basic adult dosage is two Trocinate tablets, three or four times daily, but dosage may be safely increased in severe spasm.**

Wm. P. Poythress *& Co., Inc.*

RICHMOND 17, VIRGINIA

JUST AS A REMINDER...

6 E N T *products to remember!*

AURALGAN® — IN ACUTE OTITIS MEDIA SAFE AURALGESIC AND DECONGESTANT

OTOS-MOSAN® — BROAD-SPECTRUM THERAPY IN SUPPURATIVE OTITIS

Now! BIO-TOSMOSAN® HC — IN ACUTE EXACERBATION EXTERNAL OTITIS ALLERGIC EARS

RHINALGAN® — SAFE! "NOT JUST ANOTHER DECONGESTANT"

Now! RHINALGAN® HC — ANTI-INFLAMMATORY ANTI-ALLERGIC

LARYLGAN® — FOR INFECTIOUS AND NON-INFECTIOUS THROAT INVOLVEMENTS

DOHO CHEMICAL CORP., 100 VARICK ST., NEW YORK 13, N.Y.

First emphasis is on

PAIN RELIEF

in sprains, strains, arthritis, rheumatism

not only *relieves pain* but also *relaxes taut muscles*

SAFE POTENT FAST

SOMA™

(carisoprodol Wallace)

Samples and literature on request

WALLACE LABORATORIES, Cranbury, New Jersey

A LOGICAL ADJUNCT TO THE WEIGHT-REDUCING REGIMEN

meprobamate **plus** d-amphetamine... reduces appetite...elevates mood...eases tensions of dieting...**without** overstimulation, insomnia or barbiturate hangover.

Dosage: One tablet one-half to one hour before each meal.

anorectic-ataractic

BAMADEX®

meprobamate 400 mg., with d-amphetamine sulfate 5 mg., Tablets

Lederle

FREE GENUINE ENGRAVED LETTERHEADS
DIES and PROOFS $15.00 FOR 1000
Genuine ENGRAVED STATEMENTS
RULED or PLAIN (6¼x7) $13 FOR 1000
BUSINESS ANNOUNCEMENTS
500 ONLY $20
WRITE FOR FREE PROOF
APPOINTMENT CARDS
$15 FOR 1000
DEWBERRY ENGRAVING CO.
3201-4th AVE. SO., BIRMINGHAM, ALA.

BRAWNER'S SANITARIUM

(ESTABLISHED 1910)

2932 SOUTH ATLANTA ROAD, SMYRNA, GEORGIA

For the Treatment of
Psychiatric Illnesses and Problems of Addiction

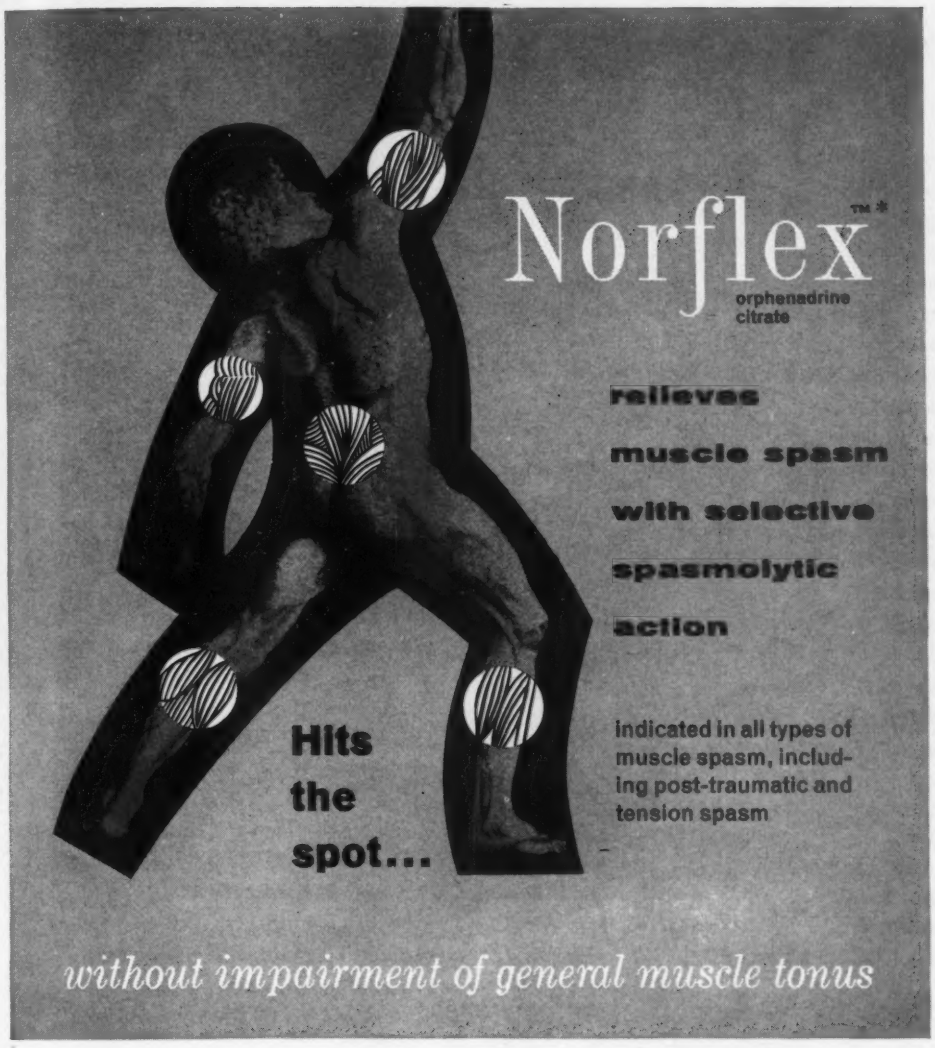
MODERN FACILITIES

Approved by Central Inspection Board of American Psychiatric Association and the Joint Committee on Accreditation

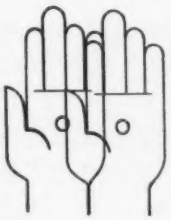
JAS. N. BRAWNER, JR., M.D.
Medical Director

ALBERT F. BRAWNER, M.D.
Associate Director

Phone HEmlock 5-4486


Norflex™*
orphenadrine citrate
relieves muscle spasm with selective spasmolytic action
Hits the spot...
indicated in all types of muscle spasm, including post-traumatic and tension spasm
without impairment of general muscle tonus

Restores mobility quickly and relieves associated pain by prompt relaxation of only the muscle in spasm. Prolonged action and potency provide all-day and all-night benefits...permitting uninterrupted sleep...facilitating rehabilitation.



standard dosage
for all adults regardless of age, sex, or weight: 1 tablet (100 mg.) b.i.d.—easily remembered... offering better patient cooperation.

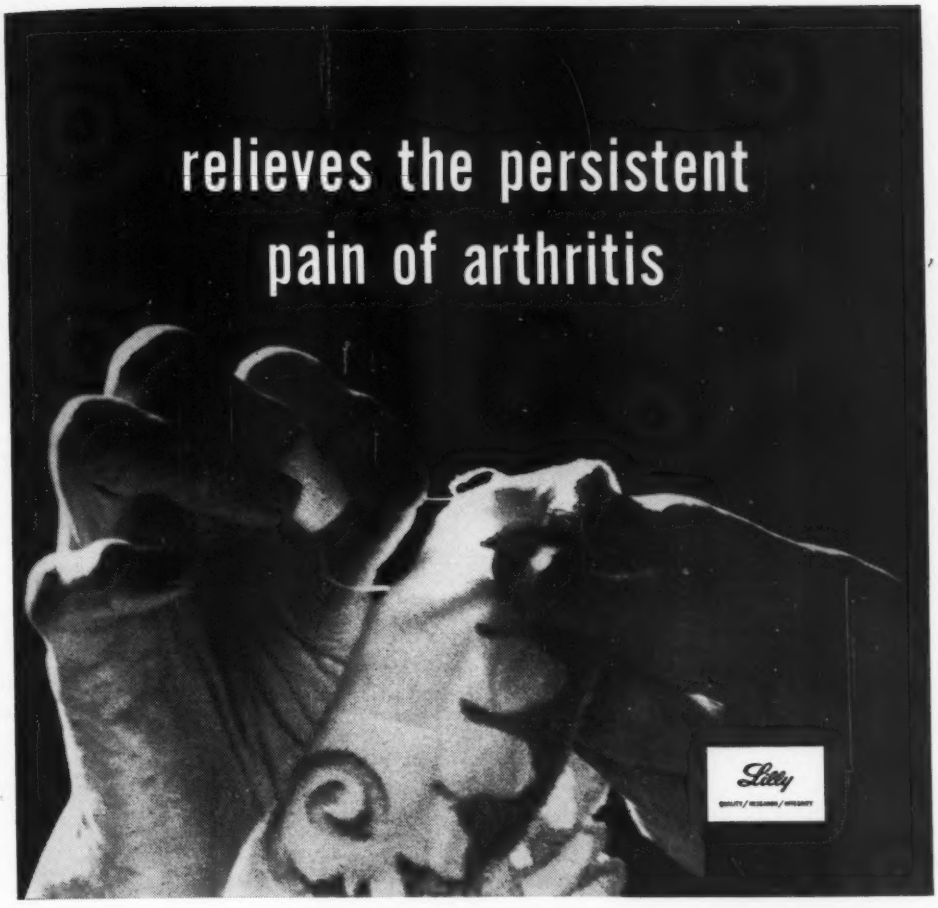
Norflex™ for prompt, safe spasmolytic action

*Trademark U.S. Patent No. 2,587,351. Other patents pending.

Northridge, California Riker

INDEX TO ADVERTISERS

ADVERTISER	PAGE
Ames Company, Inc.	60
Appalachian Hall	70
Armour Pharmaceutical Company	6, 41
Arnar-Stone Laboratories, Inc.	33
Astra Pharmaceutical Products, Inc.	opp. 64
Brawner's Sanitarium	78
Brayten Pharmaceutical Corporation	19
George A. Breon & Company	61
The Burdick Corporation	68
Ciba Pharmaceutical Products, Inc.	42, 65
Davies, Rose & Company, Ltd.	62
Dewberry Engraving Company	78
Doho Chemical Corporation	76
Eaton Laboratories	3, 23, 36, 59
Endo Laboratories, Inc.	35
Fuller Pharmaceutical Company	58
Geigy Pharmaceuticals	56
Hill Crest Sanitarium	66
Hynson, Westcott & Dunning, Inc.	48
The Janis Clinic	58
Lederle Laboratories Division, American Cyanamid Company	30, 58, 62, 68, 78
Eli Lilly and Company	3rd Cover
The S. E. Massengill Company	opp. 16, opp. 32, 55
McNeil Laboratories, Inc.	39, 54, 72
Merck Sharp & Dohme	8-9, 26, 51
Parke, Davis & Company	27, 4th Cover
Pharmaceutical Advertising Club	10
Pitman-Moore Company	2, 67
Wm. P. Poythress & Company, Inc.	75
Riker Laboratories, Inc.	1, 64, 79
A. H. Robins Company, Inc.	7, 20-21, 34, 63
Roche Laboratories, Division of Hoffmann-La Roche, Inc.	4-5, 31, 40, 52-53
J. B. Roerig & Company	37, 50
William H. Rorer, Inc.	71
G. D. Searle & Company	32, 49
Smith-Dorsey Division, The Wander Company	14-15, 38
Smith Kline & French Laboratories	17, 73
Southern Airways Company	74
First Texas Pharmaceuticals, Inc.	62
Tucker Hospital, Inc.	70
U. S. Vitamin & Pharmaceutical Corporation	28-29
VanPelt & Brown, Inc.	43
Vitamin Food Company, Inc.	66
Wallace Laboratories	12-13, 24-25, 57, 69, 77
Westwood Pharmaceuticals	18
White Laboratories, Inc.	16, 22, 44-47
Winthrop Laboratories	11



DARVON® COMPOUND

(dextro propoxyphene and acetylsalicylic acid compound, Lilly)

Darvon Compound combines the analgesic action of Darvon® with the anti-inflammatory and antipyretic benefits of A.S.A.® Compound. When inflammation is present, Darvon Compound reduces discomfort to a greater extent than does either analgesic given alone.

Usual dosage: 1 or 2 Pulvules® three or four times daily.
Also available: Darvon, in Pulvules of 32 and 65 mg.

Darvon® (dextro propoxyphene hydrochloride, Lilly)
A.S.A.® Compound (acetylsalicylic acid and acetophenetidin compound, Lilly)

ELI LILLY AND COMPANY • INDIANAPOLIS 6, INDIANA, U. S. A.

FROM PARKE-DAVIS...A NEW ORAL ANTIBIOTIC

Humatin®

KAPSEALS®

(PAROMOMYCIN, PARKE-DAVIS)

PROVIDES EFFECTIVE ANTIBACTERIAL AND ANTIAMEBIC ACTIONS. USEFUL IN INFECTIOUS DIARRHEAS OF BACILLARY AND NONSPECIFIC ETIOLOGY.[1-4] PRACTICALLY UNABSORBED, THUS VIRTUALLY NONTOXIC.[1,5-7] VALUABLE IN ALL FORMS OF INTESTINAL AMEBIASIS-ACUTE, SUBACUTE, AND CHRONIC.[1,4-7] EFFECTIVE IN PREOPERATIVE SUPPRESSION OF INTESTINAL FLORA,[4] AND IN ADJUNCTIVE MANAGEMENT OF HEPATIC COMA.[8,9,10]

Supplied: Humatin is supplied as the sulfate in Kapseals,® each containing 250 mg. of base; bottles of 16. Literature supplying details of dosage and administration available on request. *References:* (1) Courtney, K. O., & Thompson, P. E.: Paromomycin As a Therapeutic Substance for Intestinal Amebiasis and Bacterial Enteritis, Antibiotics Annual 1959-1960, New York, Medical Encyclopedia Inc., in press. (2) Godenne, G. D.: Paromomycin in Diarrheas of Infants and Children, Antibiotics Annual 1959-1960, New York, Medical Encyclopedia Inc., in press. (3) McMath, W. F. T., & Hussain, K. K.: *Pub. Health* 73:328, 1959. (4) Personal Communications to the Department of Clinical Investigation, Parke, Davis & Company, 1959. (5) Shafei, A. Z.: *Antibiotic Med. & Clin. Therapy* 6:275, 1959. (6) Elias, F. L., & Oliver-Gonzalez, J.: *Antibiotic Med. & Clin. Therapy* 6:584, 1959. (7) Carter, C. H.: *Antibiotic Med. & Clin. Therapy* 6:586, 1959. (8) Fast, B. B., *et al.: Arch. Int. Med.* 101:467, 1958. (9) Mackie, J. E., *et al.: New England J. Med.* 259:1151, 1958. (10) Stormont, J. M., *et al.: New England J. Med.* 259:1145, 1958. 05440

PARKE, DAVIS & COMPANY · Detroit 32, Michigan PARKE-DAVIS